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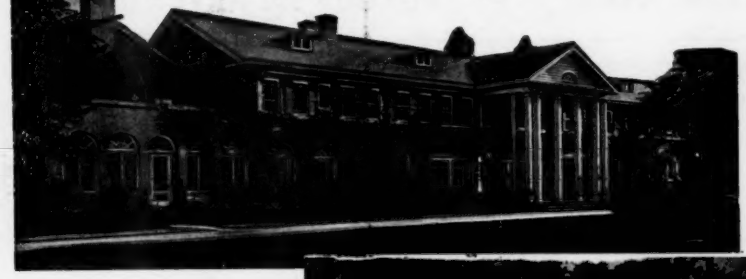

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THIRD VENTRICULOSTOMY IN TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS IN CHILDREN

HAROLD C. VORIS, M.D.
CHICAGO

HYDROCEPHALUS due to an obstruction or block in the ventricles or subarachnoid spaces is commoner in the infant than is generally supposed. A routine investigation of cases of infantile hydrocephalus will readily satisfy any one on this point. In my experience, the ratio of cases of obstructive hydrocephalus to cases of communicating hydrocephalus is about 2:1.

Patients with obstructive hydrocephalus present an obvious challenge to the neurosurgeon, for if the obstruction can be relieved or circuited the intraventricular pressure, with its damage to cerebral tissue and progressive enlargement of the head, may be brought under control. Since there are many causes of obstruction, the same procedure cannot be used or considered for all patients.

A frequent cause of obstruction or block in infantile hydrocephalus is the Arnold-Chiari malformation, associated with spina bifida in many patients, especially those with myelocele. In this condition the medulla oblongata is elongated and extends downward into the spinal canal, so that the lower end of the fourth ventricle is below the level of the foramen magnum. The cerebellar tonsils are usually elongated and extend down into the spinal canal. They, together with the lingula, are often plastered to the fourth ventricle and medulla with dense adhesions. The cranial nerves that arise from the pons and medulla are necessarily elongated, and the upper cervical spinal nerves are also elongated and run cephalad to reach their exits at the intervertebral foramens. The elongation of the medulla and cerebellum results in the blocking of the lower end of the fourth ventricle, and the adhesions of the cerebellar lingula and tonsils to the medulla and fourth ventricle obliterate the cerebellomedullary (posterior) cistern. Thus, an obstructive hydrocephalus is produced. In my experience, this is the usual cause of the hydrocephalus often associated with spina bifida. However, Ingraham, Scott and associates [1] reported only 20 cases (10 per cent) of the Arnold-Chiari malformation in their series of 546 cases of spina bifida, in 208 of which hydrocephalus was associated.

The mechanism of the malformation has been explained by Lichtenstein.[2] In spina bifida the spinal cord or membranes have an abnormal attachment to the surrounding and overlying tissues. Such an abnormal attachment may even exist (although not usually) in spina bifida occulta. It results in traction on the neuraxis

From the Mercy Hospital-Loyola University Clinics.

1. Ingraham, F. D.; Swan, H.; Hamlin, H.; Lowrey, J. J.; Matson, D. D., and Scott, H. W.: Spina Bifida and Cranium Bifidum, Cambridge, Harvard University Press, 1945.

2. Lichtenstein, B. W.: Distant Neuroanatomic Complications of Spina Bifida (Spinal Dysraphism): Hydrocephalus, Arnold-Chiari Deformity, Stenosis of Aqueduct of Sylvius, etc.: Pathogenesis and Pathology, Arch. Neurol. & Psychiat. **47**:195-214 (Feb.) 1942.

above the level of the malformation as the spinal column elongates. The more rapid growth of the spinal column than of the neuraxis is well known. The spinal cord extends the full length of the embryo during its early development, but from the fourth month the vertebral column elongates more rapidly than the cord. At birth, the tip of the spinal cord reaches only to the third lumbar vertebra, and in the adult, to the lower border of the first lumbar vertebra. Thus, any abnormal attachment of the cord, nerve roots or meninges to the spinal column or overlying parts will produce traction on the neuraxis during both prenatal and postnatal growth. In this way, not only may the medulla and cerebellum be pulled down into the spinal canal but the midbrain may likewise be elongated and pulled down into the posterior fossa. Thus stenosis of the aqueduct of Sylvius may be produced, and this may be one of the factors in the associated hydrocephalus.

Other types of congenital obstruction of the cisterna cerebellomedullaris, fourth ventricle or cerebral aqueduct exist. The foramens of Luschka and Magendie or the cerebellomedullary cistern itself may fail to develop, or a heterotopia of brain tissue may block the cerebral aqueduct. Dandy described a patient with a congenital diaphragm blocking the aqueduct.

Inflammatory obstructions are common. Not only may these block the aqueduct, fourth ventricle or cerebellomedullary cistern, but they may also involve the basilar cisterns. The latter are often the chief site of the block in most cases of meningitic hydrocephalus, which is not remediable by any surgical procedure unless it be the ventriculoureteral anastomosis recently described by Matson and Wallace.[3] Post-meningitic hydrocephalus was formerly confined to certain patients who survived epidemic cerebrospinal (meningococcic) meningitis or the terminal stages of tuberculous meningitis. With the advent of modern chemotherapy, so many patients with suppurative meningitis survive that the complications in such cases are becoming an important problem, as Bailey [4] has pointed out. Certainly, post-meningitic hydrocephalus is now seen more frequently.

Neoplasms may block the ventricular system at any point from the foramen of Monro to the fourth ventricle. They are not common in children under 2 years of age but do occur. If the tumor is in the lateral or third ventricle, it can usually be recognized in a ventriculogram; but a tumor in the posterior fossa is very difficult to differentiate roentgenographically from the various types of congenital block. Exploration of the posterior fossa often has to be carried out, unless, of course, there is a history of meningitis or the presence of spina bifida suggests the Arnold-Chiari malformation.

In order to determine whether obstruction is present in a case of infantile hydrocephalus, a dye test should be carried out, unless there is an associated spina bifida with meningocele or myelocele. In the latter case the Arnold-Chiari malformation can be assumed to be the cause of the hydrocephalus. The dye test cannot be expected to give significant results in a case of spina bifida with meningocele or myelocele, as obliteration of the spinal subarachnoid space in the region of the defect may obstruct the passage of the dye.

3. Matson, D. D., and Wallace, W. M.: Electrolyte Balance Studies in Patient with Internal Hydrocephalus After Uretero-Arachnoid Anastomosis, J. Neurosurg., to be published.

4. Bailey, P.: Chronic Leptomeningeal Thickening Following Treatment of Meningitis with Sulfa-Drugs, Ann. Surg. **122**:917-922, 1945.

A preliminary diagnostic subdural tap should precede the dye test in all cases in order to rule out subdural hematoma as the cause of enlargement of the head. In two of my cases of spina bifida and an enlarging head, subdural tap revealed a subdural hematoma.

If the diagnostic subdural tap is noncontributory, one ventricle may be entered through the open fontanel and the dye (5 cc. of 0.8 per cent indigo carmine) injected. The other ventricle should be tapped in order to demonstrate its patency and communication with its fellow. Then lumbar spinal puncture is carried out. If there is no obstruction between the lateral ventricles and the subarachnoid space, the spinal fluid will almost immediately be visibly colored with the dye. In cases of partial obstruction the dye may appear in some degree in 10 to 20 minutes. In cases of complete obstruction, the dye will fail to appear in the lumbar subarachnoid space. If there is obstruction, its site must be determined, as it may be in the third ventricle, the cerebral aqueduct, the fourth ventricle or the cisterna cerebellomedullaris.

Air studies (ventriculography) will be of great value, especially in the recognition of tumors of the third ventricle. Occasionally it may be possible to outline a neoplasm of the midbrain or the fourth ventricle by the combination of spinal and ventricular injection of air. Direct injection of the ventricles by the fontanel route is, of course, readily accomplished in most young children.

After careful study, supplemented at times by exploration of the posterior fossa, there will be cases of obstructive hydrocephalus due to the Arnold-Chiari malformation, to inflammatory block of the cerebellomedullary cistern or to an inoperable neoplasm of the fourth ventricle or midbrain, in which some type of palliative procedure to relieve the hydrocephalus is indicated.

When exploration of the posterior fossa is carried out, the procedure recommended by Torkildsen is often the obvious answer to the problem of relief of the hydrocephalus. Some type of catheter or tube is led out of one lateral ventricle through a parieto-occipital burr hole and beneath the scalp (or beneath the bone), down through the occipital muscles into the cerebellomedullary cistern, where it is anchored by suturing it to the dura. However, in inflammatory lesions such a procedure can be expected to give only temporary relief, as the tendency of the adhesions of arachnoiditis of the cisterna cerebellomedullaris to reform with recurrence of the block is well known. The Torkildsen procedure is of greatest value in cases of inoperable tumors of the upper part of the fourth ventricle, the midbrain or the posterior part of the third ventricle.

D'Errico,[5] Ritchie,[6] Steele,[7] and Adams, Schatzki and Scoville[8] have reported good results with suboccipital decompression and opening of the fourth ventricle in cases of hydrocephalus due to the Arnold-Chiari malformation, other types of

5. D'Errico, A.: The Surgical Treatment of Hydrocephalus Associated with Spina Bifida, Yale J. Biol. & Med. **11**:425-430, 1939.

6. Ritchie, W. P.: Experiences in the Treatment of Hydrocephalus in Infants, Minnesota Med. **30**:790-794, 1947.

7. Steele, G. H.: The Arnold-Chiari Malformation, Brit. J. Surg. **34**:280-282, 1947.

8. Adams, R. D.; Schatzki, R., and Scoville, W. B.: The Arnold-Chiari Malformation: Diagnosis, Demonstration by Intraspinal Lipiodol and Successful Surgical Treatment, New England J. Med. **225**:125-131, 1941.

congenital obstruction in the posterior fossa and inflammatory obstructions of the fourth ventricle or cisterna cerebellomedularis. However, in my hands, the mortality rate of these procedures in infants has been disturbingly high, and the obstruction has tended to recur in a few weeks or months. This has been especially noted in cases of the Arnold-Chiari malformation, in which I have carried out suboccipital exploration a number of times, without lasting relief of symptoms.[9]

Because of dissatisfaction with the results of exploration of the posterior fossa, ventriculostomy (establishment of a free communication between the third ventricle, and the peduncular cisterns) was given a trial in patients with obstructive hydrocephalus due to the Arnold-Chiari malformation. At first the transfrontal route, advocated by Stookey and Scarff,[10] was used. Transfrontal craniotomy was carried out, usually on the right side; the frontal lobe was elevated intradurally after preliminary ventricular tap, and the lamina terminalis was punctured above the optic chiasm. This procedure has been satisfactory in older children and adults with inoperable tumors of the fourth ventricle or midbrain, but for some reason has not worked out well in infants. Therefore a trial of the lateral approach, as described by Dandy,[11] was made. This has proved satisfactory and has been carried out in 10 patients with obstructive hydrocephalus, associated with spina bifida and presumably due to the Arnold-Chiari malformation. These 10 children have been observed from six months to four years, and the results have been excellent, with cessation of abnormal enlargement of the head and absence of increased intracranial pressure.

A small osteoplastic craniotomy in the right temporal region may be used, or, employing a musculocutaneous flap, a small subtemporal decompression may be carried out. If the intracranial pressure is high, the ventricle should be tapped before the dura is opened to avoid danger of rupture of the cortex. Then the temporal lobe is elevated intradurally. A lighted retractor or a good headlight is essential. It may be necessary to clip or coagulate one or more communicating veins between the temporal lobe and the dura. At this point it is advantageous to lower the child's head slightly. As the temporal lobe is elevated, the incisura of the tentorium can be seen. The oculomotor nerve will be seen medial to this, and anterior to it the carotid artery. Posterior to the carotid artery and medial and superior to the oculomotor nerve, the white lateral wall of the floor of the third ventricle is seen. At times the posterior communicating artery, usually hairlike in caliber, will be noted above the oculomotor nerve. This should be avoided when one is opening the floor of the third ventricle. The floor of the third ventricle is punctured with a bayonet forceps and the opening cautiously enlarged. Fluid will immediately well out of the third ventricle and may have to be removed by suction until the surgeon is satisfied with the opening. Great care must be exercised to avoid injury to the oculomotor nerve and the internal carotid artery and its branches.

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9. Voris, H. C.: Neurosurgery in Young Children, Arch. Surg. **60**:906-943 (May) 1950.

10. Stookey, B., and Scarff, J. E.: Occlusion of the Aqueduct of Sylvius by Neoplastic and Non-Neoplastic Processes with a Rational Surgical Treatment for Relief of the Resultant Obstructive Hydrocephalus, Bull. Neurol. Inst. New York **5**:348-377, 1936.

11. Dandy, W. E.: The Brain, in Practice of Surgery, edited by D. Lewis, Hagerstown, Md., W. F. Prior Company, Inc., 1932, vol. 12.

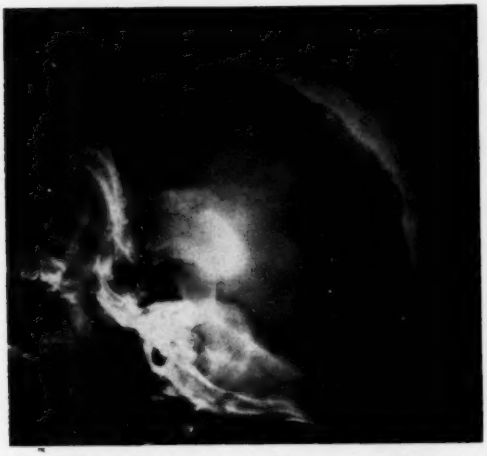

Fig. 1.—Lateral ventriculogram of L. O. made before ventriculostomy (third ventricle).

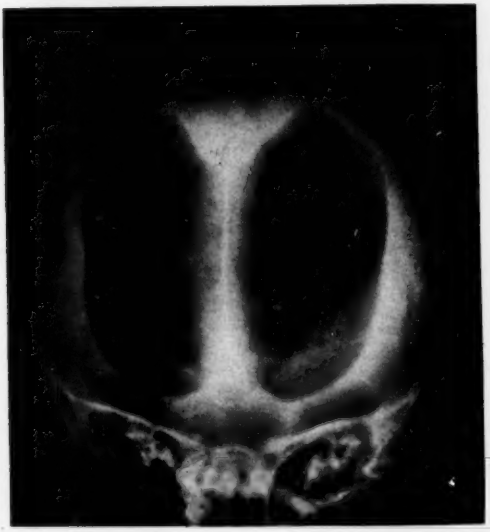

Fig. 2.—Anteroposterior ventriculogram of L. O., made before ventriculostomy.

The dura should be carefuly sutured and the wound closed in the usual way. The immediate postoperative care of the infant is similar to that of patients with craniotomy in general.

The patient on whom this procedure was first carried out, and who has consequently had the longest period of postoperative observation, will be reported on in detail.

L. O. was first seen on Aug. 31, 1946, at the age of 5 weeks. She had been born with an epithelized myelocele in the lumbosacral region. Since birth her general health and progress

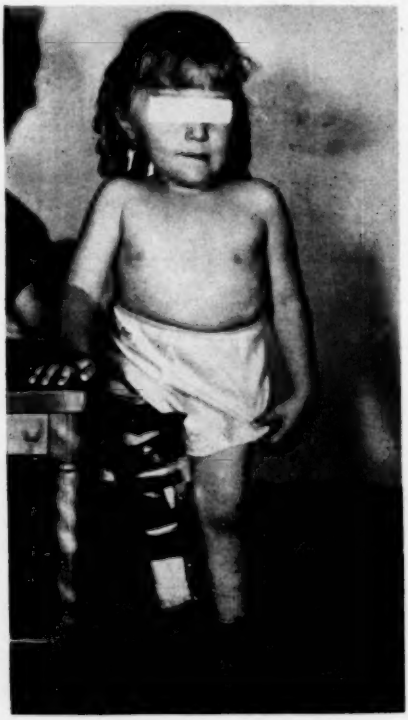

Fig. 3.—Photograph of L. O. 40 months after ventriculostomy.

had been good. She moved the left lower extremity freely but not the right, and had been observed to urinate at intervals. The circumference of the chest was 32 cm., and that of the head, 36 cm. A month later she was admitted to the hospital, and plastic repair of the large myelocele in the lumbar region was carried out on November 2. Indigo carmine which had been injected into the right lateral ventricle at the beginning of the operation was not recovered from the lumbar spinal canal during operation.

Convalescence was somewhat prolonged but satisfactory. At the time of her dismissal from the hospital, 32 days after operation, the circumference of the head was 40 cm. and that of the chest 37 cm.

Three months later the circumference of the head was 50 cm. and that of the chest 45 cm. The veins of the scalp were visibly dilated. The child was readmitted to the hospital, and a ventriculographic study was carried out. This procedure (figs. 1 and 2) revealed advanced internal hydrocephalus, but it was not felt that irreversible damage to the brain had occurred. Ventriculostomy was carried out on March 29, 1947, by the technic described above. Convalescence from this procedure was uneventful, and when the child was discharged, 11 days later, the circumference of the head was 51 cm. and that of the chest 47 cm.

A year later (March 1948) the child began to talk and occasionally stood in her crib or walker. Satisfactory voluntary control of bowel and bladder had developed. When last seen, in July 1950, 40 months after operation, she was talking well and seemed to be normal mentally. At this time she was nearly 4 years old. The circumference of the head was 56 cm., and that of the chest, 58 cm. She was able to walk between parallel bars with the aid of a brace on the right lower extremity, prescribed by the orthopedic service (fig. 3).

CONCLUSIONS

Ventriculostomy by the lateral or temporal approach is a satisfactory method of treatment in certain cases of obstructive hydrocephalus in infants or young children. It should be reserved for patients in whom the cause of the obstruction cannot be readily treated by direct surgical attack and in whom there is no evidence of obstruction of the basilar subarachnoid cisterns. In my opinion, it is the procedure of choice for infants with obstructive hydrocephalus due to the Arnold-Chiari malformation.

EEG AND CORTICAL ELECTROGRAMS IN PATIENTS WITH TEMPORAL LOBE SEIZURES

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HUGHLINGS Jackson,[1] in 1888, described a "peculiar variety of epilepsy" characterized by "exceedingly complex and very purposive seeming actions during continuing unconsciousness." Preceding these states of automatic behavior the patients were noted to have intellectual auras, or "dreamy states," with psychical hallucinations or illusions. Olfactory, gustatory or visceral auras were common. He noted that movements of mastication and salivation occurred frequently during the attack. Ten years later (1894) Jackson demonstrated by autopsy studies that such seizures were related to epileptogenic lesions in the temporal lobe, involving the uncinate gyrus and the adjacent "temporo-sphenoidal gyrus." In some cases the lesions extended into the tip of the temporal lobe and the frontal and temporal operculums.

A specific form of electroencephalogram characterized by rhythmic sharp waves and 6 per second waves was first described by Gibbs, Gibbs and Lennox [2] in 1938 as the typical electrographic manifestation of psychomotor seizures. It was originally described as a generalized bilateral discharge without reference to localized onset. The temporal origin of the electroencephalographic disturbances in most patients with this type of seizure was described by Jasper and Kershman [3] in 1941 and by Jasper,[4] with Penfield and Erickson, in 1941. From their analysis of 500 cases of epilepsy, in some of which Dr. Penfield had operated, these authors concluded that the so-called psychomotor epilepsy was not a specific form of epilepsy but merely one form of focal cortical seizure arising within the temporal lobe, though many seizures arising within the temporal lobe, with the same form of electroencephalogram, could not be described as "psychomotor." From electroencephalo-

From the Department of Neurology and Neurosurgery of McGill University and the Montreal Neurological Institute.

1. Jackson, J. H., in Taylor, J.: Selected Writings of John Hughlings Jackson, London, Hodder & Stoughton, Ltd., 1931, vol. 1 and 2.

2. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Cerebral Dysrhythmias of Epilepsy: Measures for Their Control, Arch. Neurol. & Psychiat. **39**:298-314 (Feb.) 1938.

3. Jasper, H., and Kershman, J.: Electroencephalographic Classification of the Epilepsies, Arch. Neurol. & Psychiat. **45**:903-943 (June) 1941.

4. Jasper, H. H.: Electroencephalography, in Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill., Charles C Thomas, Publisher, 1941.

graphic and clinical studies these authors concluded that "the regions primarily involved in these attacks may be within or subjacent to the temporal lobe, probably in the archipallium, or in subcortical structures related to the temporal lobe." The possibility that "psychomotor waves" may be related to subcortical lesions in some patients was also pointed out by Lennox and Brody[5] in 1946. With regard to the shifting temporal focus, they concluded that such electroencephalographic findings do not represent cortical lesions in the majority of cases, the "psychomotor waves" appearing to represent electrical activity which arises in deep brain structures and is projected to the surface. On the other hand, Walter and Dovey[6] and Cobb[7] have shown that bilateral 4 to 7 per second waves ("theta rhythm") are often related to deep-seated lesions in the general vicinity of the third ventricle.

Gibbs, Gibbs and Fuster[8] have recently provided abundant confirmation of the temporal or frontotemporal origin of the electrical disturbances in patients with psychomotor seizures, while Hill[9] found that such seizures are associated with electroencephalographic disturbances in the temporal region only twice as frequently as they are with electroencephalographic foci in other areas of the brain. The value of the use of tympanic and pharyngeal electrodes in the localization of epileptic foci on the inferior and anterior surfaces of the temporal lobe in patients with epileptic automatisms was pointed out by MacLean and Arellano,[10] thereby confirming again the original conclusion of Hughlings Jackson that this portion of the cortex is frequently the site of onset of these seizures.

In this paper, we shall present the electrographic studies on the patients reported in the paper by Penfield and Flanigin.[11] Direct cortical electrographic studies were carried out in collaboration with Dr. Penfield, as well as correlative pathological studies and follow-up observations on surgical excisions.

MATERIAL

The principal material of the present report consists of electroencephalographic and cortical electrographic studies on 91 patients operated on for temporal lobe seizures during the past 10 years. Electrographic and pathological findings are compared for these patients. Their relation to the results of surgical excision will be reported for 56 of these patients who were followed for periods of from one to 10 years after operation. In order to evaluate the importance of

5. Lennox, M., and Brody, B. S.: Paroxysmal Slow Waves in the Electroencephalograms of Patients with Epilepsy and with Sub-Cortical Lesions, J. Nerv. & Ment. Dis. **104**:237-248, 1946.

6. Walter, W. G., and Dovey, V. J.: Electroencephalography in Cases of Sub-Cortical Tumour, J. Neurol., Neurosurg. & Psychiat. **7**:57-65, 1944.

7. Cobb, W. A.: The Electroencephalographic Localization of Intra-Cranial Neoplasms, J. Neurol., Neurosurg. & Psychiat. **7**:96-102, 1944; Rhythmic Slow Discharges in the Electroencephalogram, ibid. **8**:65-78, 1945.

8. (*a*) Gibbs, E. L.; Fuster, B., and Gibbs, F. A.: Peculiar Low Temporal Localization of Sleep-Induced Seizure Discharges of Psychomotor Type, Arch. Neurol. & Psychiat. **60**:95-97 (July) 1948. (*b*) Gibbs, E. L.; Gibbs, F. A., and Fuster, B.: Psychomotor Epilepsy, ibid. **60**: 331-339 (Oct.) 1948.

9. Hill, D.: The Electroencephalographic Concept of Psychomotor Epilepsy: A Summary, IVe' Congrès international de neurologie, 1949, vol. 1, pp. 27-33.

10. MacLean, P. D., and Arellano, A. P.: Basal Lead Studies in Epileptic Automatisms, Electroencephalog. & Clin. Neurophysiol. **2**:1-16, 1950.

11. Penfield, W., and Flanigin, H.: Surgical Therapy of Temporal Lobe Seizures, Arch. Neurol. & Psychiat. **64**:491-500 (Oct.) 1950.

temporal lobe seizures in general, the electroencephalographic records of over 2,000 epileptic patients have been reviewed for comparison with the surgical cases, which received more intensive study.

PREOPERATIVE ELECTROENCEPHALOGRAPHIC STUDIES

Epileptiform abnormalities in the preoperative electroencephalogram may be divided into (*a*) those which are observed during the interval between clinical seizures and (*b*) those which occur during a clinical attack.

Abnormalities Observed Between Seizures. — The electroencephalographic records for the 91 patients with temporal lobe seizures who were treated surgically could be divided into four groups with regard to the unilateral or bilateral localization of epileptiform abnormality (fig. 1).

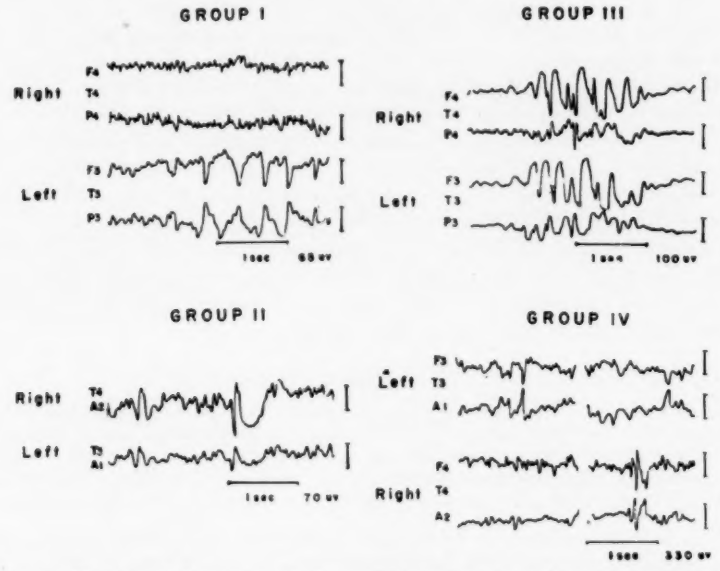

Fig. 1.—Samples of four types of electroencephalograms in patients with temporal lobe seizures. In group I the paroxysmal disturbances are localized to one temporal lobe only, without transmission to the opposite side. In group II the spikes are of higher voltage and sharper on one side, with lower voltage waves conducted to the opposite side. In group III paroxysmal discharges appear synchronously from the two temporal regions, with unilateral localization difficult or possible only with special electrodes. In group IV spikes appear alternately from one and the other temporal lobe, as though from two independent foci.

Group I: There were 31 patients (34 per cent) in whom the epileptiform discharge was consistently localized to one temporal lobe, without apparent conduction to the other side.

Group II: There were 22 patients (24 per cent) who also showed clear localization of the epileptiform discharge to one temporal lobe, but with intermittent lower voltage transmitted waves appearing from the opposite side.

Group III: There were 18 patients (19 per cent) in whom the epileptic discharge was of equal voltage and appeared synchronously from the two temporal

lobes with standard scalp leads. Localization of the focus in these patients was made possible only by the use of special basal electrodes (pharyngeal, dural or from the ala magna of the sphenoid) or by determination of the side of onset of a seizure induced with metrazol.[8]

Group IV: There were 20 patients (23 per cent) who showed a localized epileptic discharge shifting from one temporal lobe to the other even when basal leads were employed. Cases of this type have also been described by MacLean and Arellano.[10]

In groups I, II and III, representing a total of 71 cases (78 per cent), it was assumed that there was a primary cortical epileptogenic focus in one temporal lobe with varying degrees of transmission or activation of the other side. In the remaining 10 patients (22 per cent) either there was a primary focus in each temporal lobe which was capable of independent discharge, or a primary focus existed in deeper structures projected alternately or simultaneously to the two temporal regions, as suggested by Lennox and Brody.[5] Typical examples of the electroencephalographic records in each of the four groups are shown in figure 1.

Analysis of the electroencephalographic records of 428 patients with temporal lobe seizures taken from an unselected group of 2,300 epileptic patients has shown about the same percentage of unilateral as compared with bilateral localization, namely, 76 per cent unilateral. This corresponds almost exactly with the figures published by Gibbs, Fuster and Gibbs[8a] in their study of 300 patients with temporal lobe seizures. (This agreement is of particular interest in view of somewhat different methods of localization employed in the two laboratories.)

ELECTROGRAPHIC PATTERNS OF TEMPORAL LOBE SEIZURES

In many of the patients included in this series the electroencephalogram was recorded during clinical seizures which occurred spontaneously or were induced with slow intravenous injection of metrazol.[8] The electrographic pattern obtained at some time during the seizure corresponded in most cases with that originally described by Gibbs, Gibbs and Lennox.[2] This consisted of bilaterally synchronous 4 to 6 per second rhythmic waves with maximal voltage over the frontotemporal regions, a pattern confirmed by Hill[9] in a large number of cases. However, the onset of temporal lobe seizures is usually accompanied with a decrease in voltage of the electroencephalogram. This initial flattening of the record may last only five or 10 seconds before the rhythmic 4 to 6 per second waves appear, or it may continue for the greater part of the clinical seizure, even during the masticatory movements, as shown in figure 2. This type of electrographic onset was described with Daly[12] as "suppression." It was more commonly found in patients with deep anterior temporal foci but occurred also in some patients with foci on the mesial surface of the frontal lobes. Hill observed a depression in voltage at the onset of all psychomotor seizures in his series. This flattening occurred even when there were frequent high voltage spikes or sharp waves in the record immediately preceding the attack; even the focal epileptiform discharge seemed to be arrested at the onset of the clinical seizure.

12. Jasper, H. H., and Daly, D.: Suppression of the Electroencephalogram During the Onset of an Epileptic Seizure, Proceedings American Society of Encephalography, June 1947.

The electrographic onset of psychomotor seizures is in sharp contrast to the pattern of convulsive attacks arising from superficial cortical foci in areas of the convexity of the hemispheres, whose onset is marked by an increase in voltage (and usually also in frequency) of the local electrical activity. Even in petit mal seizures the high voltage wave and spike discharge precedes the sudden loss of consciousness. One may assume, therefore, that the physiological mechanisms associated with the onset of seizures arising in the deep anterior temporal region may be different than those activated by the epileptic process in many other cortical areas. The striking contrast with the electrographic pattern at the onset of the petit mal seizure is of particular interest, since the loss of responsiveness, with

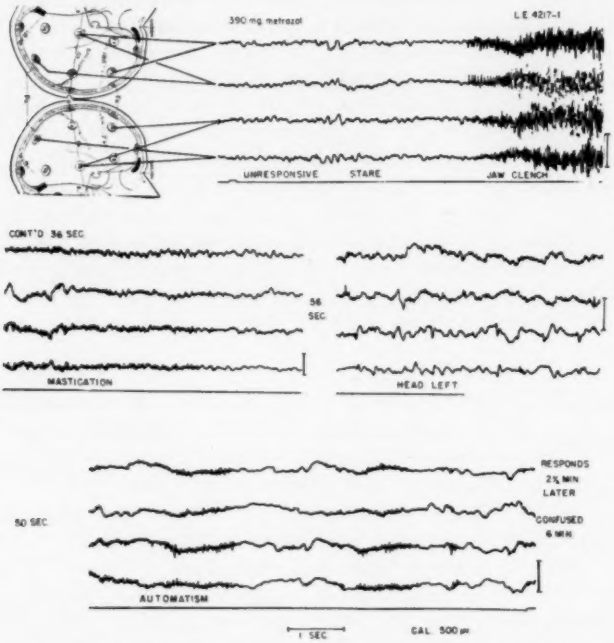

Fig. 2.—A metrazol®-induced seizure in a patient with a focus in the right temporal lobe, showing suppression of electrographic activity throughout most of the seizure. The attack consisted of masticatory movements, producing muscle potential artefacts, seen above, followed by automatic movements and mental confusion with amnesia.

assumed impairment or loss of consciousness, seems to occur during the period of suppressed electrical activity, as well as during the paroxysmal discharge, in patients with temporal lobe seizures.

Mazars [13] concluded that this apparent "extinction" of electrical activity is merely due to low voltage high frequency discharge of a true epileptic form, which he recorded in electrocorticograms, but which would not be seen in the usual

13. Mazars, G.: Interpretation du phémonène d'extinction dans la phase initiale de crises focales corticales, Electroencephalog. & Clin. Neurophysiol. **2**:343, 1950.

electroencephalograms taken through the skull and scalp. The high voltage spikes would, therefore, be absent, owing to the desynchronizing effect of a higher frequency discharge in the same area. The flattening of the electroencephalogram occurs over wide areas of both hemispheres, however, so that it seems to be more analogous to a general suppression of cortical electrical activity or to a general "arousal response," similar to the blocking of the alpha rhythm with the usual attention or a "startle" response. The unresponsive, apparently unconscious, state of the patient at the time would argue against its being an "arousal response," since this is usually associated with increased alertness, even though in some instances the experience of the aura might cause an "arousal" response. Direct cortical electrograms may shed more light on this problem.

DIRECT CORTICAL ELECTROGRAMS

Cortical electrograms were taken from the exposed temporal lobe and the adjacent parietal and frontal cortex in all the 91 patients operated on by Dr. Penfield. Operations were performed with the use of local anesthesia in all but three patients. This made possible observations on

Incidence of Electrographic Abnormalities

Form of Electrographic Abnormality	Preoperative EEG		Cortical Electrograms	
	Number of Cases	%	Number of Cases	%
Rapid spikes	37	41	52	58
Slow spikes (sharp waves)	52	57	32	35
Slow spike and wave (2-3/sec.)	12	14	17	18
2-3/sec. rhythm	27	30	32	35
4-5/sec. rhythm	8	8	2	2
6/sec. rhythm	40	43	14	15
8/sec. rhythm	3	3	..	..
10/sec. rhythm and over	1	1	..	..
Only delta waves	..	..	6	7
No abnormalities	2	3 *	..	..

the responses of conscious patients in relation to the spontaneous electrocortical activity, and the effects of electrical stimulation.

Electrographic recording was first carried out on the exposed surfaces of the temporal lobe; then, with electrodes insulated except for their tips, records were taken from the inferior surface, including the temporal tip, the uncus and the hippocampal gyrus. After removal of the tip of the temporal lobe, it was possible to record directly from the insula and, in a few instances, from the pes hippocampi through the opened ventricle. Only the general features of the results of these studies, as they apply to the subject of the present report, will be presented here.

Definite electrographic abnormalities were observed in all the patients studied, although in two patients these were seen only in the cortical electrogram. These consisted of rapid sporadic spikes (10 to 60 milliseconds in duration), slow spikes ("sharp waves," of 70 to 150 milliseconds' duration), high voltage rhythmic discharges at frequencies of 2 to 6 per second and irregular slow waves (delta waves). The incidence of each form of abnormality is shown in the accompanying table. Comparison of preoperative and direct cortical electrograms shows a higher incidence of rapid spikes in the latter, though only 58 per cent of the patients showed rapid spikes even in the cortical electrogram. The rapid spikes are more likely to represent primary focal epileptic discharge, while the more prolonged waves (slow spikes and rhythmic waves) are often due to temporal dispersion in conduction from a distant primary focus. (This may not be true always, since other

forms of primary discharge may also occur.) The slow spikes and rhythmic waves may, therefore, be recorded from areas of normal cortex into which the epileptic discharge is conducted from a distant "buried focus" (fig. 3). These secondary foci or areas are of particular importance in the temporal region, where discharges often originate at the very tip of the temporal lobe or beneath, on the uncus or hippocampal gyrus, or deep within the sylvian fissure, in the insular or peri-insular cortex. The distinction between primary and secondary foci is not always easily made unless it is possible to record from both simultaneously. If the primary focus exists in deeper, inaccessible structures which have fairly direct connections with the temporal lobe, it is possible to mistake a secondary for a primary epileptic discharge. In most of the patients in this series, however, the persistence of the neurosurgeon in exploring deeper structures has finally led to what seemed to be a true primary focus in or adjacent to a gross pathological lesion, even though the initial electrograms taken showed only secondary discharges from apparently normal cortical tissue.

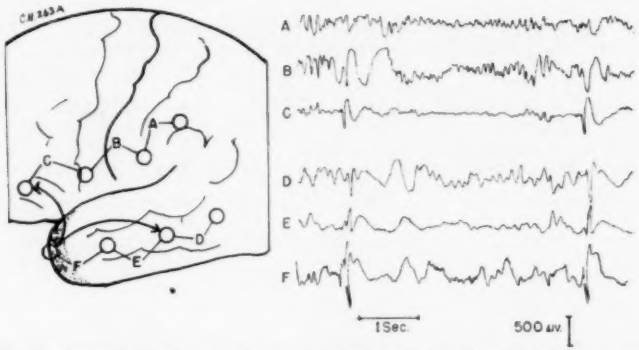

Fig. 3.—Electrocorticogram of a patient with post-traumatic focus of spike potentials from the tip of the temporal lobe, showing conduction of spikes posteriorly and anteriorly to the frontal operculum.

Focal rapid or slow spikes appeared spontaneously in 84 of the 90 cases in this series (93 per cent). In a few patients minimal amounts of metrazol® were administered by slow intravenous injection to increase the spiking without inducing a seizure. The use of barbiturate narcosis was not necessary and was avoided in order to maintain a responsive patient and to observe the results of electrical stimulation unmodified by the effects of the drug. A few of the patients did tend to go to sleep at the end of the procedure, but the "sleep waves" seemed to confuse, rather than clarify, the electrographic picture.

Local electrical stimulation was of assistance in many cases, especially when the onset or entire seizure, typical of the patient's habitual attacks, was reproduced. Electrical after-discharge often took the form of rhythmic high voltage waves at 2 to 3 or 5 to 6 per second, sometimes only from a local area near the site of stimulation but often with conduction to other parts of the temporal lobe. The mechanism of spread frequently did not show the gradual progression, such as characterizes the spread of after-discharge in other areas of the cortex. After a

short local after-discharge at the site of stimulation, high voltage rhythmic waves would suddenly break out over the entire temporal region. This is illustrated in the following case of an epileptic automatism produced by local stimulation of the uncus (fig. 4) to be reported. Description of this case in some detail may shed light on mechanisms operating in these seizures.

CASE J. O.—*Olfactory aura followed by automatism.*

A man aged 20 had had seizures during the past six years which were ushered in by an olfactory aura, consisting of a smell like burning oil. After this he would pass into a confused state of automatic behavior and unintelligible speech, which might last for some time. There was no significant event in his past history which might explain the onset of these attacks, and neurological examination revealed no abnormality. The pneumoencephalogram disclosed a relative enlargement of the left temporal horn of the lateral ventricle.

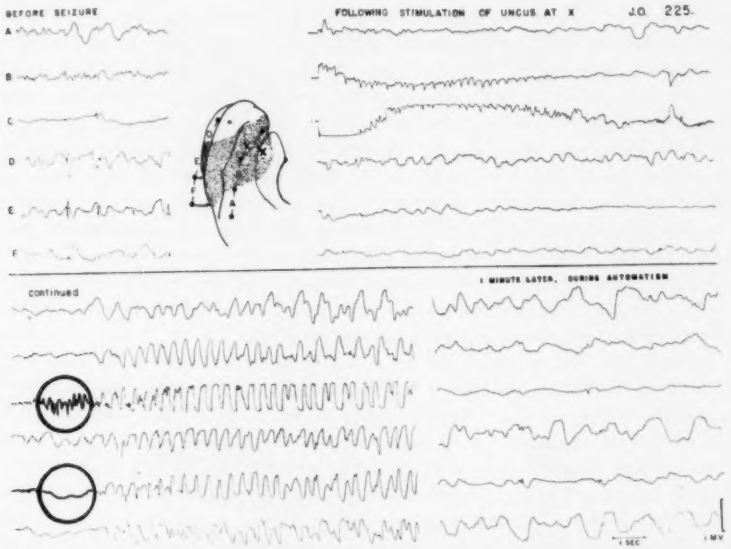

Fig. 4.—Electrocorticogram of patient J. O., described in text, with an area of spontaneous spikes from the inferior temporal region (stippled). Electrical stimulation of the uncus at *X* produced a clinical epileptic automatism, shown in the electrocorticogram by rapid discharges from near the site of stimulation, with suppression of spikes and other cortical activity over the temporal lobe for 16 seconds after the end of stimulation. Inset circles show the record amplified three times, demonstrating rapid activity only near the site of stimulation and a flat line from the lateral surface of the temporal lobe. Suddenly high voltage 3 per second waves appeared from all leads and then as suddenly disappeared, with low voltage slow waves taking their place. The automatism continued through the postictal phase of apparent cortical exhaustion.

Preoperative electroencephalographic study showed sporadic slow spikes and 4 to 6 per second waves, which were maximal over the left anterior temporal region and from the left pharyngeal electrode, with transmitted spikes and rhythmic waves to the opposite side. At the onset of a clinical seizure the spikes disappeared and the record became flat for a time, followed by a high voltage 4 to 6 per second rhythmic discharge, first maximal from the left frontotemporal region but rapidly spreading to become synchronous and of equal amplitude from the two hemispheres. These results were considered consistent with a deep-seated epileptogenic lesion in the anterior temporal region. This diagnosis was confirmed by the electrocorticogram shown in figure 4.

At operation, the cortex of the temporal lobe itself seemed normal, but the uncinate gyrus was tough and atrophic. The patient's olfactory aura, followed by his characteristic form of seizure, was reproduced by electrical stimulation of the uncus. The anterior 4 cm. of the temporal lobe was removed, including the uncinate gyrus. The postexcision electrogram showed residual spiking posterior to the area excised, in the second temporal convolution, but further excision was not carried out because of the danger of affecting speech. A few low voltage slow spikes were also recorded in the postoperative electroencephalogram, and the patient claimed to have experienced his aura on one occasion but has not had a recurrence of his former seizures.

In this case we have demonstrated what seems to happen during the course of an epileptic automatism of temporal origin (fig. 4). There was an initial period of low voltage rapid local discharge, which would certainly not be detected in the usual EEG record with scalp surface electrodes, as Mazars [13] has pointed out. However, during this time the electrical activity from the entire temporal region was suppressed. Even the spikes which had previously been recorded from the lateral surface of the temporal lobe disappeared. The patient stated that he had his olfactory aura during this time, and he then became unresponsive. Shortly after the appearance of high voltage 4 per second discharges recorded from all electrodes on the inferior and lateral surfaces of the temporal lobe (they might well have appeared from the opposite side as well had we been recording from there), the patient began to swallow and turn his head to the right and began aimless automatic movements, moving his arms around and around over each other, as in his habitual seizures. After the active paroxysm, the electrogram showed the low voltage irregular slow waves characteristic of postictal exhaustion, but the patient continued his confused automatic behavior for 90 seconds. Amnesia was complete for the principal portion of the seizure and for many seconds of the postictal period, but the olfactory aura was recalled.

It seems that this sequence of events may be described in terms of three stages: (1) focal epileptiform discharge in the vicinity of the uncinate gyrus, with general suppression of electrical activity in the rest of the temporal lobe (and possibly of other cortical areas as well); (2) activation of temporal rhythmic system (possibly via subcortical projection systems), during which time normal functions of the temporal lobe may undergo paroxysmal paralysis, and, finally, (3) depression of function of the temporal lobe through the ganglionic exhaustion of the postictal state. During the first stage the patient may experience an aura, though its trace may be obliterated by retrograde amnesia should the attack be a severe one. Temporal lobe functions seem to be impaired by different mechanisms. The clinical manifestations of these "psychoparetic" states may appear similar throughout (Penfield and Jasper [14]).

The cortical area of sporadic spikes was not usually restricted to a very small zone, but oftener involved several square centimeters of cortical surface, such as the entire tip of the temporal lobe, the uncus and the anterior third of the hippocampal and fusiform gyri. Frequently partial excision of such an area would be followed by more intense spike discharge from the remaining portion. Such areas usually corresponded to rather extensive cortical atrophy, as judged by the appearance and consistency of the excised tissue, although frequently the area of spikes extended beyond the area of cortex which Dr. Penfield considered to be grossly abnormal.

14. Penfield, W., and Jasper, H. H.: Highest Level Seizures, A. Research Nerv. & Ment. Dis., Proc. **26**:252-271, 1947.

COMPARISON OF PATHOLOGICAL AND ELECTROGRAPHIC LOCALIZATION IN RELATION TO TYPE OF PREOPERATIVE ELECTROENCEPHALOGRAM

The 12 patients with tumors of the temporal lobe were considered apart from those with atrophic lesions for this aspect of the study. It is of interest that none of the patients with tumors showed a shifting localization from one side to the other (group IV) in preoperative electrographic studies. Eight of the 12 showed strictly unilateral abnormality (group I); 2 showed clearly maximal discharge

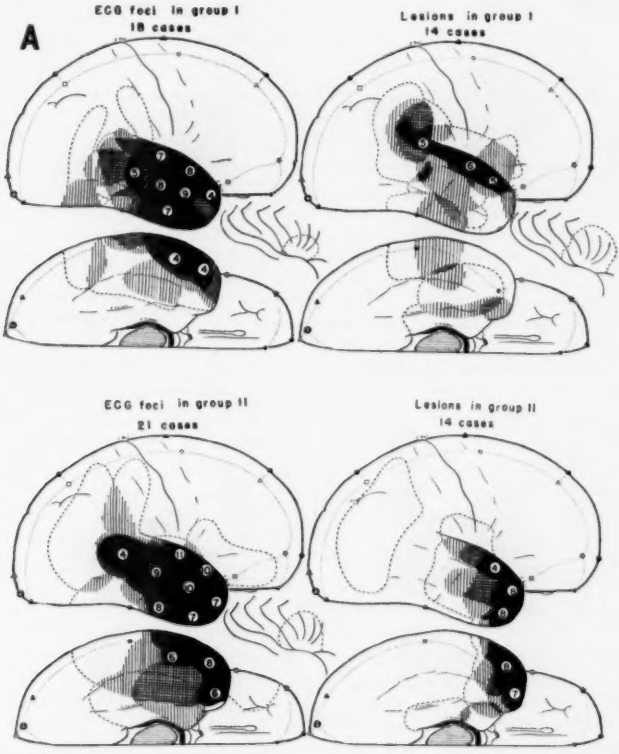

Fig. 5.—Summary of the electrographic foci and objective lesions in all patients according to their preoperative electroencephalographic classification. *A*, strict unilateral (group I) and unilateral transmitted (group II) activity.

from one side with intermittent lower voltage conducted waves from the opposite side (group II), and 2 showed bilaterally synchronous rhythmic temporal discharge with unilateral localization evident only with special procedures (group III).

Only 55 patients with both gross and microscopic evidence of atrophic lesions are considered here. The extent of the apparent atrophy, as drawn by Dr. Penfield at the time of the operation, was summarized on a composite brain map. Likewise, the areas of local epileptic discharge, as mapped from cortical electrograms, were summarized (fig. 5). The accuracy of these maps can be only approximate, but the

areas in black where there is overlapping of the localization in four or more patients may be considered fairly reliable. The areas of atrophy are perhaps more reliable than the electrographic localization, since complete detailed electrographic exploration of the inferior surfaces was not carried out in all cases and in many cases the electrographic localization was extended by conduction from the primary focus to adjacent cortex.

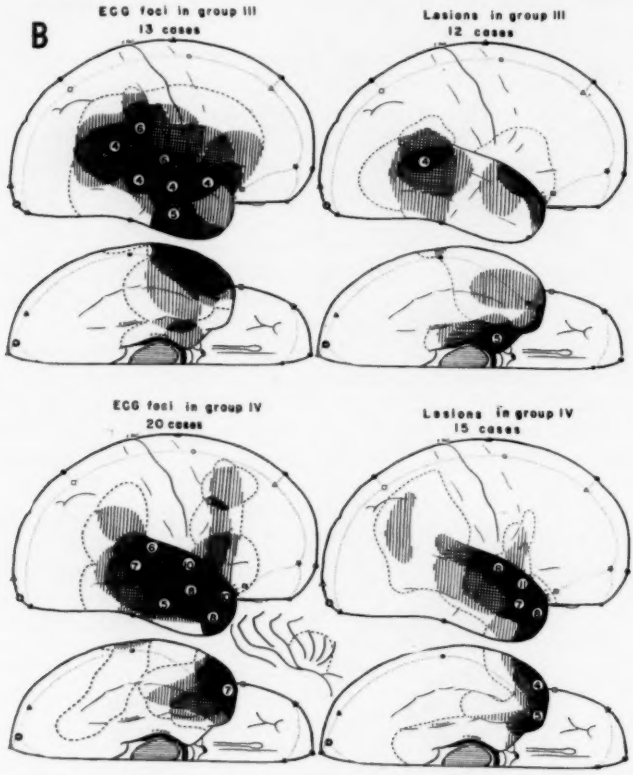

Fig. 5 (cont.).—*B*, bilateral synchronous (group III) and bilateral independent (group IV) discharges.

In the patients with strictly unilateral preoperative electroencephalographic localization (group I, fig. 5 *A*) the cortical electrographic foci were found principally over the lateral surface of the middle and anterior portions of the first, second and third temporal convolutions. Objective lesions in these patients were concentrated in the first temporal gyrus, with very little involvement of the tip of the temporal lobe, uncus and hippocampal system. In patients with transmitted bitemporal disturbances (group II, fig. 5 *A*) and secondary bilaterally synchronous rhythms (group III, fig. 5 *B*) the lesions were concentrated on the tip of the temporal lobe and the adjacent uncus and hippocampal gyrus, the electrographic

localizations being less clearly differentiated. There seemed to be two concentrations of lesions in patients with prominent secondary bilaterally synchronous rhythms (group III), one in the uncus and adjoining peri-insular portion of the temporal pole and another in the posterior temporal region in the vicinity of the angular gyrus. Lesions or foci involving the cortex of the insula itself do not seem to produce prominent bilateral electrographic disturbances.

Definite pathological lesions of the temporal cortex were also found in patients whose preoperative electroencephalogram suggested a bilateral temporal focus. In some of these the secondary focus on the opposite side persisted after operation and resulted in the recurrence of seizures arising from the opposite temporal cortex, as illustrated in the case of C. H.

CASE C. H.—*Epileptic automatisms and convulsive seizures due to post-traumatic temporal lesion.*

A man aged 37 received a blow to the vertex in the right parietal region six years prior to his admission, while in the Canadian Merchant Marine. His history was otherwise without significance. Three months later the attacks began; they had always been of the same type. He turned a little pale, his pupils dilated and he seemed confused. He was apt to say, "It is caught," or "It shows," from which his wife knew that he was going to have an attack. He continued to walk or to drive an automobile and would stop and pull up to the side when his wife told him to. At such times he usually made swallowing movements. When a major convulsive seizure developed, he turned his head slowly to the right, his pupils dilated and his eyes turned to the right. There was blinking of both eyelids, followed by movements of all extremities, more pronounced in the arms than in the legs, and one arm was raised. During this time he opened and closed his mouth. His wife did not recall his having been aphasic after a seizure. The neurological examination revealed nothing abnormal.

The pneumogram showed the ventricles to be symmetrical and only slightly enlarged. There was definite enlargement of the left inferior horn.

The electroencephalogram showed bilateral temporal disturbances with bursts of 4 to 6 per second rhythms, alternating with isolated sharp waves (fig. 6). Localization was made at the pharyngeal electrodes with shifting of activity from one side to the other. With dural electrodes in both temporal regions, a more persistent abnormality appeared in the left temporal area, as shown in figure 6.

Surgical exploration of the left temporal lobe was carried out by Dr. Penfield in October 1948. A traumatic scar was found on the under surface of the temporal pole. Cortical electrograms revealed high voltage rapid spikes from a local area adjacent to the scar, with conducted slow spikes recorded from the second and third temporal convolutions posteriorly, as shown in figure 6*C*. The patient's attack could not be reproduced by electrical stimulation. A 3 per second electrical after-discharge followed stimulation of the temporal pole. The spikes appeared spontaneously without any form of activation. The anterior end of the temporal lobe was then amputated and the electrogram repeated. There were no further spikes from adjacent tissue.

The electroencephalogram taken seven days after the operation showed no epileptiform abnormality, and there was even no significant delta abnormality near the operative site. A good electrographic prognosis was given, and it was assumed that the bilateral electrographic disturbances seen in the preoperative electrogram must have been secondary to the focus seen in the left temporal region.

The patient had no further attacks during his stay in the hospital. One year later he lost consciousness while out hunting with a friend and apparently shot off a whole box of cartridges aimlessly without knowing it. This may have been an attack, though no one saw it. He was returned for examination. While the electroencephalogram was being recorded, a typical seizure was induced with hyperventilation, which began with local 5 per second rhythmic spikes maximal from the right pharyngeal electrode (fig. 6*D*). It was apparent that at this time the patient had seizures arising from the temporal lobe opposite the one removed.

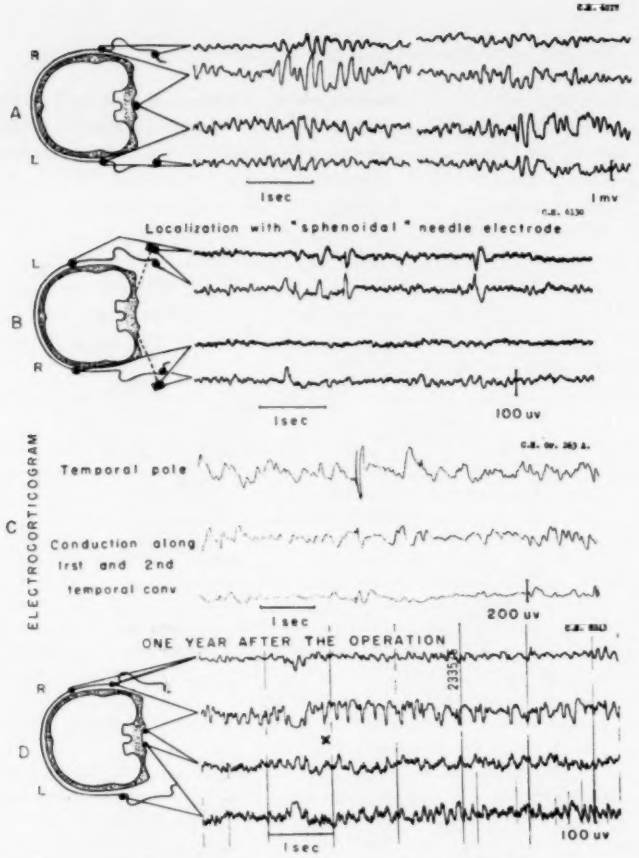

Fig. 6.—Preoperative electroencephalogram (*A* and *B*), electrocorticogram (*C*) and postoperative electroencephalogram (*D*) of patient C. H., with recurrence of contralateral temporal focus one year after removal of the temporal lobe on one side (see text for description).

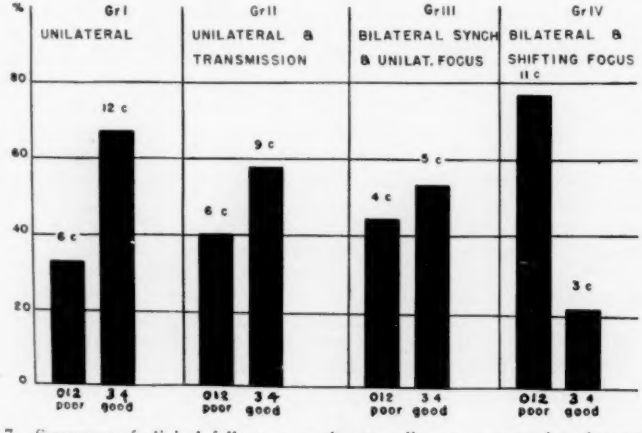

Fig. 7.—Summary of clinical follow-up results according to preoperative electroencephalographic classification.

RELATON OF TYPE OF ELECTROENCEPHALOGRAM TO RESULTS OF SURGICAL EXCISION

The results of the follow-up study reported in the preceding paper, by Penfield and Flanigin,[11] were used in the attempt to determine whether or not the type of preoperative electroencephalogram might aid in an estimation of the probabilities of successful surgical therapy. For this purpose the follow-up ratings 0, 1 and 2 were combined into one for the patients whose seizures had recurred after operation, even though some were considered 50 per cent improved. The two "success" groups, rated 3 and 4, were also combined to include those who were cured or over 75 per cent improved. The incidence of good and poor results according to the clarity of unilateral localization in the preoperative electroencephalogram is shown in figure 7.

It is clear from this graph (fig. 7) that the incidence of good surgical results declines progressively with the clarity of unilateral electrographic localization. With strictly unilateral electrographic abnormalities in the preoperative tracing, 67 per cent of the patients showed good results, while in the group with a "shifting focus" only 21 per cent had good follow-up results.

RELATION OF COMPLETENESS OF EXCISION OF ELECTROGRAPHIC FOCUS TO FOLLOW-UP RESULTS

One might expect that the degree of success of surgical excision of an area of cortex giving rise to epileptiform discharge would be related to the completeness with which all of the electrically abnormal tissue was removed. In 32 cases the electrographic focus, as determined by direct recording during the operation, was thought not to have been completely removed. In 22 cases removal of the electrographic focus was judged to have been complete. The incidence of successful postoperative results was higher (59 per cent) in the group thought to have had a complete excision of the electrographic focus (fig. 8). However, there were many (38 per cent) successful results in the group with incomplete excision, so that remaining cortical tissue capable of giving rise to electrographic abnormality does not always imply a poor clinical result.

In order to obtain data of more specific significance for the electrographic studies, the follow-up results were tabulated in a different way than were the 0 to 4 rating of Penfield and Flanigin. For all patients who had a recurrence of any portion of their preoperative pattern of attacks after operation the result was considered a technical failure, even though their attacks were of such a minor character (e.g., only an aura) that the operation would be considered a clinical success. This was done because a small discharging focus, sufficient to show clearly in the electrogram, might produce a minor aura without ever giving rise to a major seizure. For patients with no attacks the results were, of course, considered successful, while for those who had seizures of a totally different form the result was also considered successful from the point of view of the surgical procedure with respect to the previous habitual seizures. In these cases one might assume that the area of cortex giving rise to the previous form of seizure had been removed. Grouping the patients in this manner, we find a more definite relation to the completeness with which the electrographic focus was removed, as shown in figure 9.

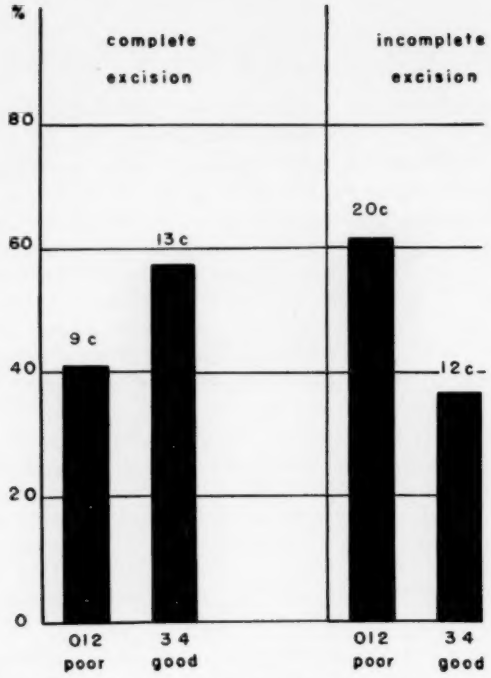

Fig. 8.—Summary of clinical follow-up results, depending on completeness of excision of the electrocorticographic focus.

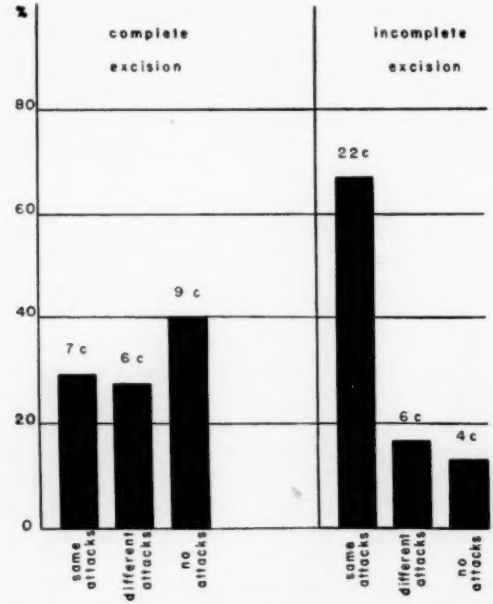

Fig. 9.—Summary of follow-up results according to completeness of excision of electrocorticographic focus in patients who had a recurrence of any portion of attacks similar to those which had occurred preoperatively, in those who had recurrence of seizures of a different form and in those who had no postoperative seizures.

Only 31 per cent of the patients with complete excisions had a partial or complete recurrence of their habitual attacks after operation, while 69 per cent of the patients with partial excisions had such a recurrence. Forty per cent were completely free of seizures of any form in the group with electrographically complete excisions, while only 12 per cent were completely free of attacks in the group not having a complete excision of their electrographic focus.

RELATION OF FOLLOW-UP RESULTS TO ELECTROGRAPHIC PROGNOSIS

On the basis of the completeness of excision of the electrographic focus, and judged by the amount of abnormality recorded in the postoperative electroencephalogram, an attempt was made to predict the degree of success to be expected from the operation. A rating scale of 0 to 4 was used in the attempt to compare it with the success rating of Penfield and Flanigin. All electrographic ratings were given independent of knowledge of the follow-up results. It was

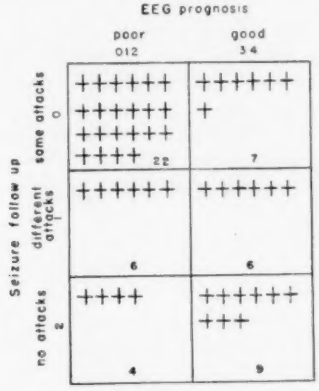

Fig. 10.—Scatter diagram of the relation of the prognosis to the recurrence of seizures after operation.

found that there was only a chance relation between the two sets of ratings; prognosis on the basis of the electroencephalogram was of no value in predicting the actual clinical success of the operation, as judged by these methods of rating.

With the revised rating according to recurrence of any portion of the previous pattern of seizures, there was a significant correlation between the electroencephalographic prognosis and these postoperative results, as shown in figure 10; but there were many exceptions. Four patients were given a poor electroencephalographic prognosis who have had no postoperative seizures, and 9 patients with a good electrographic prognosis have had at least a partial recurrence of their preoperative seizures. In the group in whom a different form of seizures developed after operation, half received a good electrographic prognosis and half a poor one, a purely chance relationship. With reference to the preoperative seizures only, there were 31 patients (74 per cent) for whom the electrographic prognosis was correct.

On most of these patients postoperative electroencephalographic studies were carried out three or four weeks after the operation, at the time of the patient's discharge from the hospital. It is apparent that such records are of limited value because the acute reactions to the operative procedure had not completely subsided and changes in the cortical tissue about the operative site which occur after the patient's discharge from the hospital are probably more important with regard to recurrence of seizures than is the condition three to four weeks after operation.

COMMENT

Epileptic seizures arising within the temporal lobe (including the insula and uncinate-hippocampal systems) occur in about one of every five patients with epilepsy. They represent about one half of all patients with seizures which seem to be of focal cortical origin. Their relatively high incidence, together with important relations to mental disease, makes them of particular interest and importance, as emphasized by Gibbs [15] and his co-workers. The results of the present study are in general agreement with the findings of these authors.

The electroencephalogram gives definite confirmatory evidence for the temporal origin of these seizures in nearly all cases, if adequate examination procedures are employed. We have found slow intravenous injection of metrazol® the most effective method of activation in these, as in other epileptic, patients, especially since it makes possible a correlation between the aura or onset of the patient's attack and changes in the electroencephalogram. Sleep activation has not been as successful in our hands as it has for Gibbs and his colleagues, though our experience with this method has been limited.

Although localization over the temporal or frontotemporal region was clear in nearly all confirmed cases, electrographic evidence for a primary focus in only one temporal lobe was difficult or impossible in 38 of the 91 patients operated on (42 per cent). Review of the electrographic records from 428 patients with temporal localization (of over 2,000 epileptic patients examined in the electroencephalography department during the past three years) showed about 40 per cent in which lateralization was difficult or impossible. In almost half the patients operated on the bilateral electrographic localization seemed to be due to the localization of a unilateral epileptogenic lesion in the temporal cortex which was capable of epileptic activation of both temporal lobes with remarkable facility. This seems especially true with atrophic lesions of the uncus and hippocampal system, often including the peri-insular portion of the temporal pole and possibly also an area of cortex in the posterior temporal portion of the operculum in the vicinity of the angular gyrus. Unilateral excision of these areas in some cases has resulted in the disappearance of the electrographic abnormality from both temporal lobes.

It seems clear, therefore, that unilateral cortical epileptogenic lesions are likely to be found in the majority of patients with temporal lobe seizures (about 75 per cent). The results of unilateral surgical therapy in these patients is much better than in those in which a unilateral electrographic localization cannot be established. In this remaining 25 per cent of the cases, with shifting and bilaterally equal and synchronously discharging temporal foci, the contralateral electrographic focus may

15. Gibbs, F. A.: Ictal and Non-Ictal Psychiatric Disorders in Temporal Lobe Epilepsy, J. Nerv. & Ment. Dis., to be published.

persist after excision of an apparent focus on one side, and clinical seizures recur in most cases. In some cases this has been true when a gross atrophic lesion was found on the side of operation. One must assume, therefore, that such lesions may exist on both sides, though Dr. Penfield has not as yet undertaken operative exploration of both temporal regions. Such lesions might occur as a result of contusion of both temporal poles due to head injury, or possibly of local birth ischemia.

One must consider also the possibility that local temporal epileptiform discharge may represent in some cases secondary activation of temporal cortex via projection fibers from a primary epileptic process in deeper structures. The experimental results recently reported with Ajmone-Marsan, Stoll and Jasper [16] have demonstrated that epileptiform spikes and sustained after-discharges can be set up in the tip of the temporal lobe in the cat and monkey by local application of strychnine to, or electrical stimulation of the septal nuclei and specific local areas of the thalamus and basal ganglia. Temporal discharges may appear either unilateral or bilateral from such indirect activation. It must be concluded, therefore, that, although the majority of temporal seizures seem to arise from primary epileptogenic lesions of the cortex of the temporal lobe, some could arise from more deeply situated structures.

It was pointed out by Penfield and Flanigin that not more than one-half the patients with temporal lobe seizures included in this study had attacks of confusion and automatic behavior which might fulfil the definition of psychomotor epilepsy given by Gibbs. Forty-one of the 88 patients (46 per cent) included in this study had attacks of automatic behavior. Attacks of confusion and automatic behavior are also produced in some patients by focal epileptogenic lesions in other cortical areas, particularly the frontal, as pointed out by Hill [9] and others. The location of the foci in patients with automatism, as judged by direct cortical electrographic records and by electrical stimulation of the exposed cortex, was more frequently found in the temporal pole, uncus and anterior portion of the insula, though in some cases the focus was clearly more posteriorly situated in the temporal lobe. We have been unable to distinguish the electrographic tracing in patients with temporal lobe automatisms from those with other forms of temporal lobe seizure. Consequently, it would seem better to speak of temporal lobe seizures for patients with focal epilepsy of temporal origin as judged by the electroencephalogram.

Automatism or psychomotor attacks are, therefore, only one form of temporal lobe seizure. If it is only a matter of definition, and if the word "psychomotor" is preferred, with the understanding that it includes all forms of temporal lobe seizure, the implication of the term may be understood; but it becomes somewhat confusing to the clinician if the seizures consist only of an epigastric aura followed by a generalized convulsion. The distinction between focal cortical seizures and pyschomotor seizures is also confusing, since the latter is also most frequently focal cortical. The greatest difficulty arises, however, when the term psychomotor is used to describe a form of electroencephalogram, without reference to localization. Sharp waves and 4 to 6 per second waves may characterize the epileptiform

16. Ajmone-Marsan, C.; Stoll, J., and Jasper, H. H.: Electrophysiological Studies of Sub-Cortical Connections of the Tip of the Temporal Lobe, Electroencephalog. & Clin. Neurophysiol. **2**:356, 1950.

discharge from any region of the cortex, and consequently this pattern may be associated with a wide variety of seizures, the form alone having little specific relation to the kind of clinical attack. We favor abandoning the term psychomotor in favor of the term behavior automatisms, or temporal automatisms if there is definite evidence of a focal onset within the temporal lobe.

SUMMARY

The results of preoperative and postoperative electroencephalographic studies, as compared with direct cortical electrograms, have been described for 91 patients operated on for temporal lobe seizures. Follow-up studies over a period of one to 10 years were available on 54 of these patients. In about three of four patients with temporal lobe seizures there was clear evidence in the preoperative electroencephalogram of a focus of onset in one temporal region. In such cases the surgical excision of the epileptogenic lesion, guided by the cortical electrogram, resulted in decided improvement or cure of seizures in about two of three cases. In about 25 per cent of the cases the preoperative electroencephalogram did not show a consistent unilateral focus of epileptiform discharge, but, rather, revealed a focus shifting from side to side, or bilaterally synchronous discharges. Prognosis was poor after unilateral temporal lobe excisions in these cases.

Less than one-half the patients with temporal lobe seizures had attacks of automatic behavior which might be described as "psychomotor." The cortical electrogram recorded during such attacks showed an initial suppression of electrical activity, followed by high voltage rhythmic waves at 3 to 6 per second, and then a postictal period of exhaustion with low voltage slow waves. The mental confusion and automatic behavior appeared the same during the ictal and the postictal phase of the seizure, suggesting a common impairment of temporal lobe function in these attacks, but impairment due to different mechanisms at different stages of the seizure.

PERMANENCY OF GLUTAMIC ACID TREATMENT

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OUR PREVIOUS publications have been concerned with the effect of glutamic acid on mental functioning at various levels of the learning curve and over different intervals of time.[1] Glutamic acid was found to be beneficial not only to patients in the category of low-defective intelligence, but to persons at the high-defective and borderline intelligence levels, who were within striking distance of average intelligence.[2]

Once this improvement had been secured and a limit, or "ceiling," established, it was natural for us to turn our attention to the problem of the permanency, or carry-over effect, of treatment with glutamic acid following cessation of therapy. Our present paper, therefore, is a report of our findings to date after glutamic acid therapy had been discontinued from 2½ to three years.

Of the 69 children and adolescents in our original study,[1b] 38 who received glutamic acid treatment were available for psychological retesting after the cessation of therapy for an interval of 2½ to three years. All the 38 patients had received six months, and 24 of them one year, of treatment before glutamic acid therapy was discontinued. Seventeen of our present group have epileptic seizures. Twenty-one are mentally retarded but do not have convulsions.

The 38 patients we are reporting on at present were included in our original group, but we have considered all psychological test results separately for them so as to obtain a more accurate evaluation of the permanent effect of glutamic acid therapy over a period of years. Table 1 gives the initial test data for our present group prior to glutamic acid treatment and their retest scores following six months of glutamic acid therapy.

At the beginning of treatment the average chronological age of our children and adolescents was 11 years 8 months, and their average mental age was 7 years 1 month, giving an intelligence quotient of 61.58 (table 1). This quotient falls at

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From the Department of Child Neurology, Columbia University College of Physicians and Surgeons, and the Neurological Institute of New York.

1. Zimmerman, F. T.; Burgemeister, B. B., and Putnam, T. J.: (*a*) Effect of Glutamic Acid on Mental Functioning in Children and in Adolescents, Arch. Neurol. & Psychiat. **56**:489-506 (Nov.) 1946; (*b*) A Group Study of the Effect of Glutamic Acid upon Mental Functioning in Children and Adolescents, Psychosom. Med. **9**:175-183, 1947; (*c*) Ceiling Effect of Glutamic Acid upon Intelligence in Children and in Adolescents, Am. J. Psychiat. **104**:593-599, 1948.

2. Zimmerman, F. T., and Burgemeister, B. B.: Effect of Glutamic Acid on Borderline and High-Grade Defective Intelligence, New York State J. Med. **50**:693-697, 1950.

the defective intelligence level. After six months of therapy their mental age was raised to 8 years 3 months, indicating a gain of 14 months in six months, which is more than twice the acceleration expected of a child with average intelligence (6 months in six months) and much faster than their own former rate of development. The average intelligence quotient for the group was raised from 61.58 to 68.42 points, or a gain of 6.84 points during the first six months of therapy. The retest quotient was also nearer the borderline level of intelligence, which is 70 to 79 points.

Statistical analysis of results (table 1) shows 93 chances in 100 of a genuine difference between initial and retest verbal intelligence test scores after six months of treatment. On the performance test the average quotient was raised from 62.90 to 67.89 points, or 4.99 points, after six months of therapy. The chances of a genuine difference in performance retest scores are slightly lower than those obtained on verbal test material, namely, 81 in 100.

TABLE 1.—*Psychological Test Scores Prior to Glutamic Acid Therapy and Retest Scores Following Six Months of Treatment*

			Initial Scores				Retest Scores						
Test	No.	C. A.*	M. A.*	I. Q.	σ	σ_{av}	M. A.	I. Q.	σ	σ_{av}	D/σ dif.	Points Change in I. Q.	Chances of a Real Difference
Stanford-Binet.....	38	11 yr. 8 mo.	7 yr. 1 mo.	61.58	18.81	3.06	8 yr. 3 mo.	68.42	20.88	3.39	1.50	+ 6.84	93 in 100
Performance.....	..	.....	7 yr. 3 mo.	62.90	21.90	3.56	8 yr. 2 mo.	67.89	26.53	4.31	0.89	+ 4.99	81 in 100

* C. A. and M. A. indicate chronological and mental ages, respectively.

TABLE 2.—*Initial Intelligence Test Scores of Patients Completing One Year of Treatment and Their Quotients Following Six Months and One Year of Therapy*

Test	No.	I. Q. 1	I. Q. 2	I. Q. 3	Total Point Gain
Stanford-Binet....	24	62.96	70.00	71.25	7.04 + 1.25 = 8.29

As we reported previously,[1c] the greatest gain on verbal intelligence retest scores seems to occur during the first six months of therapy, and a limit, or "ceiling," tends to be reached after one to 1½ years. Table 2 gives the initial intelligence quotients of the 24 patients in our group who completed one year of glutamic acid treatment and their intelligence quotients following six months and one year of treatment, respectively.

As may be seen from table 2, the intelligence quotient was raised 7.04 points during the first six months of therapy and only 1.25 points during the second six months, making a total gain of 8.29 points for the entire treatment period. These data are in keeping with the results obtained in our larger group [1c] and indicate that a ceiling is rapidly being approached on the verbal intelligence test material after one year of therapy.

Performance test results (table 3), in contrast to the verbal intelligence retest results, show almost as much acceleration during the second six months of treatment as during the first six months. When we reported on the larger group, of 69 patients,[1c] the acceleration on the nonlanguage test was actually greater for the second six month interval.

Table 3 indicates a gain of 5.00 points in the performance quotient after six months of glutamic acid treatment for our group of 24 patients who were given one year of therapy and a gain of 4.59 points during the second six month treatment period, making a total gain of 9.59 points for the year. It is of interest that while the gain on motor tests during the first six months is less than the gain obtained in verbal intelligence, the net gain for the year of therapy is greater on motor tests than on the verbal intelligence material. This is because the "ceiling effect" noted on verbal intelligence retests is not apparent on performance tests during the second six months of treatment, increases being almost equal for the two intervals. In the present group close to a 10 point gain for the treatment period of one year raises the average performance quotient from the defective to the borderline intelligence classification.

TABLE 3.—*Initial Performance Test Scores and Quotients (P. Q.) Following Six Months and One Year of Treatment*

Test	No.	P. Q. 1	P. Q. 2	P. Q. 3	Total Point Gain
Performance.....	24	62.91	67.91	72.50	5.00 + 4.59 = 9.59

TABLE 4.—*Initial Intelligence and Performance Test Scores Before Glutamic Acid Treatment and Those at an Interval of Two and One-Half to Three Years After Cessation of Therapy*

			Initial Scores				Retest Scores						
Test	No.	C. A.	M. A.	I. Q.	σ	σ_{av}	M. A.	I. Q.	σ	σ_{av}	D/σ dif.	Point Change in I. Q.	Chances of a Real Difference
Stanford-Binet.....	38	11 yr. 8 mo.	7 yr. 1 mo.	61.58	18.81	3.06	9 yr. 3 mo.	64.74	22.15	3.61	0.67	+ 3.16	74 in 100
Performance.....	..	.....	7 yr. 3 mo.	62.90	21.90	3.56	9 yr. 2 mo.	64.48	25.74	4.18	0.46	2.50	67 in 100

After the treatment period administration of glutamic acid was discontinued completely, and none of our present group of 38 patients has received any glutamic acid for an interval of 2½ to three years.

In table 4, psychological test results are given for the entire group of 38 patients at the beginning of glutamic acid treatment and after glutamic acid medication had been discontinued 2½ to three years. Fourteen patients in our group received six months of treatment, and 24 of them received one year of therapy, before medication was stopped. Thus the group receiving six months of treatment had received no medication for three years, and the group receiving one year of therapy had had no medication for 2½ years, since the treatment interval. The group chronological age had increased 3½ years since the beginning of treatment, having risen from 11 years 8 months to 15 years 2 months.

Psychological testing was identical for the two groups; i. e., the group receiving only six months of treatment was retested after the cessation of therapy for six months, at the time when the one year group was completing treatment, so as equate the practice effect.

According to table 4, the entire group now shows a gain of 3.16 points over the pretreatment intelligence quotient following the cessation of therapy for 2½ to three years. There are 74 chances in 100 that this gain is a genuine one. If the

increase in intelligence quotient after six months of treatment is considered (table 1), it may be seen that the group has held almost one-half the initial rise in intelligence quotient (6.84 points) obtained under therapy.

Performance tests give a proportionate increase, with a net gain of 2.50 points for the group and with 67 chances in 100 of a real difference following the cessation of treatment for 2½ to three years.

Results to date show, therefore, a considerable degree of permanency after glutamic acid treatment has been discontinued over a period of years. It must also be pointed out that the range of improvement under treatment was large (up to 20 points) and that this gain is not apparent when an average figure is given. Many of these patients have held their large treatment gain remarkably well during the 2½ to three year interval following the cessation of glutamic acid therapy.

When we obtained our first post-treatment results, we hypothesized[3] that adequate dosage and degree of initial improvement under therapy were important factors determining permanency. Our present data confirm this assumption. We also postulated that a higher degree of permanency was associated with a longer treatment interval—one year, for example, rather than a six month period. We

TABLE 5.—*Intelligence Test Results Using Length of Treatment as the Criterion of Differentiation*

Treatment Period	No.	I. Q. 1	I. Q. 2	Post-Treatment I. Q.	Point Gain	
					On G. A. *	No. G. A.
Six months.....	14	62.86	68.57	63.57	+5.71	−5.00 =
					+0.71	
One year.....	24	62.96	70.00	65.41	+7.04	−4.59 =
					+2.45	

* G. A. stands for glutamic acid.

have therefore divided our present group into two parts on the basis of length of treatment in order to see whether differences in degree of permanency can be demonstrated by this criterion. Results of the verbal intelligence tests for the six month and the one year treatment group appear in table 5.

Since only 14 and 24 cases comprised the two groups, respectively, generalizations must be made with caution. It may be noted from table 3, however, that there is little difference in rate of loss between patients receiving six months and those receiving one year of treatment as judged from their retest intelligence quotients 2½ to three years after cessation of treatment. The one year treatment group does show very slight greater permanency than the six month group (a 4.59, as compared with a 5.00 point loss), but differences are negligible. It must also be remembered that the six month group has been without medication for three years, whereas the one-year group has been without treatment only 2½ years. In view of this advantage to the one-year group, we believe that evidence from our small sample does not point toward greater permanency on verbal intelligence scores in the one-year group. Results indicate that on verbal material the amount of gain is of greater importance in determining permanency to date than is length of treatment.

3. Zimmerman, F. T., and Burgemeister, B. B.: The Techniques, Dynamics and Permanency of the Glutamic Acid Treatment of Mental Retardation, Education **70**:410-418, 1950.

Performance test findings, on the other hand, appear to give results which favor length of treatment as a positive factor in determining permanency. Data are shown in table 6.

Increase in performance tests ratings during the first six months of therapy was identical for the two groups, namely, 5.00 points. At present the six-month post-treatment group shows a slight loss over the pretreatment group (— 0.71 point), whereas the one-year group still maintains a net gain of 3.34 points. We believe, therefore, that the continued improvement in the performance test during the second six months of treatment (4.59 points) favors length of treatment as a determinant of permanency, especially since the two groups showed the same amount of gain during the first six month interval and had the same amount of practice.

TABLE 6.—*Performance Test Quotients Using Length of Treatment as the Criterion of Differentiation*

Treatment Period	No.	P. Q. 1	P. Q. 2	Post-Treatment P. Q.	Point Gain	
					On G. A.*	No. G. A.
Six months.....	14	62.85	67.85	62.15	+5.00	−5.70 = −0.70
One year.....	24	62.91	67.91	66.25	+5.00	−1.66 = +3.34

* G. A. stands for glutamic acid.

TABLE 7.—*Effects of Glutamic Acid on Mental Function as Found by Four Investigators*

Authors	Changes in I. Q. Under Treatment *	
	Controls	Experimental
McCulloch [4]	+	−
Kerr and Szurek [5]	3 mo. − 6 mo. +	− +
Loeb and Tuddenham [6]	+	+
Ellson, Fuller and Urmston [7]	+	+

* The plus sign indicates an increase in the intelligence quotient; the minus sign, a decrease.

COMMENT

Other investigators who have studied the effect of glutamic acid on mental functioning have not yet reported on permanency following cessation of treatment and are still conducting experiments along the lines of our previous work. Four groups of investigators have not agreed with our findings. When their various results are tabulated graphically, interesting facts emerge.

As may be seen from table 7, in McCulloch's study,[4] the average intelligence quotient for the experimental group under glutamic acid treatment fell in the absence of treatment, while the average for the control group rose. Kerr and Szurek [5] obtained decreases in the intelligence quotient for both their control and their experimental subjects at the end of three months of therapy and increases

4. McCulloch, T. L.: The Effect of Glutamic Acid Feeding on the Cognitive Abilities of Institutionalized Mental Defectives, read before the American Association on Mental Deficiency, New Orleans, 1949.

5. Kerr, W. J., Jr., and Szurek, S. A.: Effect of Glutamic Acid on Mental Function: Pilot Study, Pediatrics **5**:645-647, 1950.

after six months. Loeb and Tuddenham [6] and Ellson, Fuller and Urmston,[7] on the other hand, report an average rise for the experimental group, as well as for the control group, after treatment.

Tabulation of results shows that these investigators do not agree among themselves with respect to the absence of permanent effect, and such inconsistency in results points to the possibility of differences in type and adequacy of medication, among other things, as an explanation.

One of the major criticisms of our work, for example, has been the knowledge on the part of the testing psychologists that medication was being given. Ellson, Fuller and Urmston [7] commented on this and stated that the objection was met by their experiment in which the "psychometrist" was informed that only one-half the group was receiving therapy. After the publication of these reports, we conducted experiments in which the factor of suggestion was eliminated by withholding from the psychologist any information as to whether the patients were receiving treatment or not. We feel that the experimental technic of some of the observers mentioned above fails to rule out this factor and that no knowledge of treatment should have been available to the "psychometrists" if they wished to validate their hypothesis. In addition, their use of the term "psychometrist" rather than "psychologist" could be taken to designate an incompletely trained worker, such as a university student. The words "psychometrist" and "psychologist" have distinctly different connotations as to degree of training.

The nature of our controls has also been criticized by other investigators. We used a technic whereby progress under glutamic acid treatment was evaluated by individual matching of the person's performance with his own scores on several pretreatment intelligence and performance tests. We still believe that such a procedure, which involves matching the subject with himself, provides a more satisfactory kind of control series than one in which a subject or group is matched with another, unknown individual or group. Loeb and Tuddenham make quite a point of this in their article [6] and imply that gains we obtained may have been due to faulty controls. In their work, however, they concede that "the pretreatment performance of the control group was by no means identical with that of the experimental group but the method of statistical analysis utilized makes appropriate allowance for the initial differences between groups in evaluating their gains." In addition, their groups were not matched for chronological age. It is our opinion that differences in initial potentiality for learning between two groups cannot adequately be corrected by statistical technics, that statistical technics were not designed as a subsitute for technical precision and that unless the groups are accurately equated at the beginning, results are invalid.

Two, and possibly three, of the four groups who reported a decrease in the intelligence quotient with glutamic acid did not use glutamic acid at all, but gave sodium glutamate, orally, which, however, they designated as "neutralized glutamic acid"—a phrase which subtly implies that both compounds are identical by drawing the mind and eye to the words "glutamic acid." The same investigators likewise used the term "glutamic acid" in the title of their papers, rather than the more accurate term "sodium glutamate."

6. Loeb, H. G., and Tuddenham, R. D.: Does Glutamic Acid Administration Influence Mental Function? Pediatrics **6**:72-77, 1950.

7. Ellson, D. G.; Fuller, P. R., and Urmston, R.: The Influence of Glutamic Acid on Test Performance, Science **112**:248-249, 1950.

We know from considerable experience that it is not an easy task to administer insoluble, unpleasant-tasting glutamic acid orally to children. It is quite understandable that investigators would seek a less onerous way of carrying out this experiment. That the sodium salt of glutamic acid, or sodium glutamate, is soluble, is widely known. We used glutamic acid rather than sodium glutamate from necessity rather than choice. Our own experience with sodium glutamate is decidedly at variance with that of other investigators. In the early days of our experiments we substituted sodium glutamate for glutamic acid, without the knowledge of either the children receiving it or their parents. Approximately 175 pounds of 200 pounds (79.4 of 90.7 Kg.) distributed simultaneously were returned, and in each instance the distraught parent stated that it caused violent gastric distress and vomiting when administered in a quantity identical with that of the glutamic acid. Only two parents of the entire group were able to administer the sodium glutamate.

Two investigators to date have obtained results similar to ours with carefully controlled experiments. Recently, Sister Maureen of Catholic University,[8] in her doctoral dissertation, has expressed complete agreement with our results in terms of a rise in intelligence quotient and improvement in personality, as measured by a more elaborate battery of intelligence and personality tests, including the Rorschach test.

The most recent study comes from Bessman,[9] a physician and fellow of the Research Foundation of Children's Hospital, Washington, D. C. He has conducted biochemical and clinical studies on glutamic acid for the past few years under a grant from the United States Navy (Office of Naval Research). Bessman reports:

> Experiments using a control group have shown a significant improvement in the intelligence quotients of mentally deficient children treated with glutamic acid. Although there have been several negative reports as to the effectiveness of this treatment, it appears that if cases are selected according to the criteria of the original investigators, results similar to theirs can be obtained. This conclusion is based on the study of over 150 children for a period of two years or more. The oldest child tested was 14 years of age; most of the subjects were younger.[9]

Bessman likewise states that children with a grossly damaged brain give little or no response to treatment. This is in agreement with our own findings and criteria in the selection of cases. We stated[2] that patients showing gross damage to the brain, as indicated by a particular Rorschach configuration, do not respond as well to treatment as a group as do those without such damage.

Albert, Hoch and Waelsch,[10] of course, secured results similar to ours in a preliminary report some time ago. Levine[11] and Quinn and Durling,[12] more recently, have also obtained results similar to those reported by us.

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8. Harney, Sister Maureen: Some Psychological and Physical Characteristics of Retarded Children—Before and Following Treatment with Glutamic Acid, Doctoral Dissertation, Catholic University of America, Washington, D. C., 1949.

9. Bessman, S.: Glutamic Acid Is Food for Thought, Research Reviews, Office of Research, United States Department of the Navy, December 1950.

10. Albert, K.; Hoch, P., and Waelsch, H.: Preliminary Report on the Effect of Glutamic Acid Administration in Mentally Retarded Subjects, J. Nerv. & Ment. Dis. **104**:263-274, 1946.

11. Levine, E. S.: Can We Speed up the Slow Child?, Volta Rev. **51**:269-270, 1949.

12. Quinn, K. W., and Durling, D.: Twelve Months' Study of Glutamic Acid Therapy in Different Clinical Types in an Institution for the Mentally Deficient, read before the American Association for Mental Deficiency, New Orleans, 1949.

Glutamic acid has been used extensively on the Continent, but references to it do not find their way readily into American journals. To date, however, we know of four groups of investigators who have obtained results similar to ours on a qualitative basis.

Bakwin [13] reports giving small daily doses of glutamic acid and observing in the subjects treated the disappearance of motor hyperactivity, better social adaptability, enrichment of vocabulary and more affective tractability. Penta,[14] using a combination of glutamic acid and pyridoxine (vitamin B_6), noted improvement in 10 mental defectives in social adaptability, in motor skills and in affect. Levi and Falorni [15] more recently treated 10 mental defectives with the same combination of drugs and verified their results by psychological tests. Improvement in level of intelligence and in motor skill was apparent. Schachter,[16] a physician on the Committee of Marseilles on childhood deficiency and a research fellow at the National Institute of Hygiene, reports positive results in his study in which glutamic acid was added to thyroid extract or vitamin B complex and given to 87 children. To date, results reported are limited to 23 of the patients treated.

Schachter states that in 16 of the 23 children, or 69 per cent of those treated, he could note satisfactory results after an average period of therapy of 14 months. In addition to his observation, reports of parents and teachers were included in the evaluation of results. In two cases findings were also confirmed by results in the Binet-Simon intelligence test.

SUMMARY

Our results show a considerable degree of permanency after glutamic acid treatment has been discontinued over a period of years, with many patients holding their gains on the intelligence test remarkably well. Our data indicate that amount of gain on the verbal intelligence test is of greater importance in determining the permanency of effect than is length of treatment. Performance test findings, however, favor length of treatment as a positive factor determining the degree of permanency.

The results of investigators who have obtained negative results with the administration of glutamic acid can be explained by the lack of technical precision, both in the proper administration of the drug and in experimental accuracy. When these factors have been handled adequately, results similar to ours have been obtained, both in the human and in the animal fields. The latter is well demonstrated by Albert and Warden [17] in a study in which a problem box much more elaborate than our maze was used. This particular experiment has never been challenged, or even repeated. Among psychologists, of course, it is well known that problem box work is much more laborious and time consuming than are the relatively rapid maze experiments.

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13. Bakwin, H.: Glutamic Acid and Mental Functioning, J. Pediat. **31**:702-703, 1947.

14. Penta, P.: Osservazioni su frena stenici trattati con acido glutamico e piridoxina. Progr. med., Napoli **5**: 1949.

15. Levi, S., and Falorni, M. L.: Controllo psicol. di frenastenici trattati con acido glutamico e pirodoxina, Riv. clin. pediat. **7**:429-448, 1950.

16. Schachter, M.: L'acide glutamique en neuro-psychiatrie infantile: Premiers resultats d'une experience clinique 1947-1950, J. d. practiciens Jan. 4, 1951.

17. Albert, K. E., and Warden, C. J.: The Level of Performance in the White Rat, Science **100**:476, 1944.

THE SYNDROME OF CROCODILE TEARS

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IT IS, of course, well known that the efferent impulses causing the lacrimal gland to secrete leave the lacrimal nucleus in the brain stem by preganglionic fibers of the parasympathetic nervous system which run in the nervus intermedius of Wrisberg, the greater superficial petrosal nerve and the vidian nerve (nervus canalis pterygoidei) and enter the sphenopalatine ganglion. The postganglionic fibers, arising here, reach the lacrimal gland through the zygomatic and lacrimal nerves.

Any lesion affecting this pathway may cause a disturbance in the secretion of tears, which usually parallels alterations in the secretion of saliva and the sensation of taste and which may consist of cessation, diminution or exaggeration of lacrimation. In fact, Köster [1] (1900, 1902) noted such disturbances in 41 of his 62 patients with paralysis of the facial nerve. In 29 cases tearing was either completely abolished (15 cases) or diminished (14 cases), whereas in 12 cases excessive lacrimation was observed. Cases of Bell's palsy with either absence or profuse lacrimation were also reported by Lutz [2] (1931). On the other hand, the morbid condition of unilateral lacrimation when the patient eats or drinks certain foods, which is not to be confused with the often very annoying tearing in Bell's palsy, is rather uncommon. In the latter, the paralytic ectropion allows the tears to run out of the conjunctival sac.

This phenomenon, first noted by Oppenheim [3] (1913), and Engelen [4] (1913), was described in more detail by Bogorad [5] (1928), who called it the syndrome of crocodile tears.[6] His case was that of a young girl who complained that when-

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1. Köster, G.: Deutsches Arch. f. klin. Med. **68**:343 and 505, 1900; **72**:327 and 518, 1902.
2. Lutz, A.: Arch. f. Ophth. **126**:304, 1931.
3. Oppenheim, H.: Lehrbuch der Nervenkrankheiten, Basel, S. Karger, 1913.
4. Engelen, cited by Oppenheim.[3]
5. Bogorad, F. A.: Vrach. delo. **11**:1328, 1928.
6. The notion that the crocodile, a harmful reptile, will weep over a man's head after he has devoured the body and then will eat up the head too was the theme of one of the many "scientific" anecdotes of Pliny the Elder. It was popularized in the fourteenth century by the "Travels of Sir John Mandeville." This gentleman-explorer existed only in the imagination of Jean de Bourgogne, a French physician, who himself never left his country and who, charmingly enough, confessed that had these fantastic tales he relates been told him, he would not have believed them (Legouis, E.: A History of English Literature: The Middle Ages and the Renascence, vol. 1, London, J. M. Dent & Sons, Ltd., 1948). All that has apparently not deterred Kroll (Kroll, M.: Die neuropathologischen Syndrome, zugelich Differentieldiagnostik der Nervenkrankheiten, Berlin, J. Springer, 1929) from believing that the phenomenon "an die Tränen erinnert, welche das Krokodil beim Verzehren der Beute vergiesst."

ever she ate or drank the eye on the side of the previously total facial paralysis overflowed with tears, although she neither wept for joy nor shed bitter tears on this side. At the time that lacrimation during eating appeared the recovery of the motor paralysis was complete.

In Kaminsky's[7] (1929) two cases a similar phenomenon was observed about three weeks after the facial nerve became paralyzed; in the first case it followed an operation on the ear, and in the second it was probably *e frigore*. In the second case the paralysis of the face cleared completely three weeks after its onset, whereas in the first the recovery was slower and less definite, leaving behind a "tic" in the previously paralyzed angle of the mouth. The first patient, who at the time of observation had been shedding crocodile tears since the age of 18 years, did it only while eating salty or sour foods. There was no lacrimation when she took sweet or bitter foods, masticated without food or swallowed fluids. When distressed, she wept only on the normal side. There was no relation between the degree of temperature of the food and the amount of tears shed for salty and sour morsels, and she did not lacrimate when the anterior two thirds of her tongue was pricked with a needle. At the time of observation the second patient had been afflicted with the syndrome of crocodile tears for three years; it appeared before his recovery from the motor paralysis, being observed whenever he ate any food but not when he chewed without food and only slightly when he swallowed fluids.

In Ford's[8] (1933) four cases of complete facial paralysis, persisting for several months, return of voluntary movements in the face was accompanied with facial contracture, abnormal associated movements and lacrimation on the affected side whenever the patient ate, or even took any sapid substance into the mouth, but never in other circumstances. In his first patient, who sustained a trauma to the head, the paroxysmal lacrimation, as he called it, appeared 10 months after the injury and, at the time of observation, had lasted 16 years. Any substance with a strong flavor produced tearing, but chewing or voluntary movements of the face did not. In the second patient lacrimation during eating developed six months after sudden paralysis of the face and was still present two years later. Sour apples or hot soup caused more tearing than did other foods. Appetizing odors, as well as mechanical stimulation of the inside of the mouth, had the same effect, but there was no weeping under other conditions. The third patient had congenital syphilis. Five months after sudden paralysis of the seventh nerve he began to shed crocodile tears whenever he ate. During the examination he became despondent and wept several times equally on the two sides. The fourth patient was operated on by Dr. W. E. Dandy for Ménière's syndrome. As the acoustic nerve was found firmly adherent to the facial nerve, both nerves had to be sectioned. During the resulting paralysis of the face the eye was dry on the affected side, but five months later the patient began to shed the crocodile tears whenever he ate solid food. If he gulped liquids down quickly, the eye remained dry. In all of Ford's cases, the sense of taste was preserved, and the lacrimation began when the functional recovery was not complete, but had just started.

7. Kaminsky, S. D.: Deutsche Ztschr. f. Nervenh. **110**:151, 1929.

8. Ford, F. R.: Paroxysmal Lacrimation During Eating as Sequel of Facial Palsy: Syndrome of Crocodile Tears, Arch. Neurol. & Psychiat. **29**:1279 (June) 1933.

Tumarkin [9] (1936) mentioned having seen 13 cases of the syndrome but presented no histories of the disease, whereas Ford and Woodhall [10] (1938) reported another case of paroxysmal lacrimation, coupled with associated movements and an increase of tone in the facial musculature, occurring while the patient ate foods with strong flavor but not under other conditions. They also mentioned having seen a similar syndrome in several cases of neurosyphilis, in which the lesion was probably in the segment of the nerve which lies within the subarachnoid space, as well as in one case of vascular disease associated with subarachnoid hemorrhage and in three cases of facial palsy complicated by herpes zoster of the ear. Savin [11] (1939) reported three cases. In the first the patient wept while eating appetizing food. At the time of appearance of paroxysmal lacrimation, his facial paralysis had almost completely recovered, but there were some associated movements of the face when the patient whistled. Taste sensation was lost during paralysis but was normal when shedding of the crocodile tears began. In the second case the tearing was associated with synkinesias in the previously affected side of the face. In the third case there were contracture of the facial muscles, pronounced synkinesias and evident signs of injury to the chorda tympani, as for some years the affected side of the tongue had felt as though it were made of india rubber.

In the first of the two cases reported by Russin [12] (1939) severe trauma of the head, causing paralysis of the right facial nerve, was followed several months later by paroxysmal lacrimation when the patient ate sour, salty or bitter foods. When the crocodile tears first appeared, 15 years before the time of observation, the patient could not innervate any one of his facial muscles without innervating to some degree the total facial musculature, the tonus of which was increased. The sensation of taste was preserved on both sides. Substances with strong flavor and masticatory movements had no effect on lacrimation. In the second case the syndrome appeared several months after trauma to the head, which caused paralysis of the seventh and ninth cranial nerves, as well as hypesthesia over the ophthalmic division of the fifth cranial nerve.

Christoffel's [13] (1939) patient, who had recovered only partially from paralysis of the seventh cranial nerve and who had contracture of the orbicularis oculi muscle on the affected side, began to lacrimate while eating right at the onset of the paralysis. He was accustomed to wear an eyeglass on the side which became paralyzed, taking it out during his meals. When, once, he forgot to do so, no tears appeared during eating. Consequently, he continued to wear the eyeglass at mealtime, and this apparently liberated him from his troublesome syndrome, which he had had for four years.

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9. Tumarkin, I. A.: Proc. Roy. Soc. Med. **29**:1685, 1936.

10. Ford, F. R., and Woodhall, B.: Phenomena Due to Misdirection of Regenerating Fibers of Cranial, Spinal and Autonomic Nerves: Clinical Observations, Arch. Surg. **36**:480 (March) 1938.

11. Savin, L. H.: Brit. J. Ophth. **23**:479, 1939.

12. Russin, L. A.: Paroxysmal Lacrimation During Eating as a Sequel of Facial Palsy: Syndrome of Crocodile Tears, J. A. M. A. **113**:2310 (Dec. 23) 1939.

13. Christoffel, H.: Schweiz. med. Wchnschr. **69**:455, 1939.

McGovern [14] (1940), as cited by Boyer and Gardner [15] (1949), reported a case of paroxysmal lacrimation, and Gottesfeld and Leavitt [16] (1942) treated a patient with injections of alcohol into the sphenopalatine ganglion, with arrest of lacrimation for about five months. Bing [17] (1947) observed three cases of paroxysmal lacrimation, or "gustolacrimal reflex," as he has called the syndrome since his first observation in 1924. In two of the cases the paralysis of the seventh cranial nerve was caused by a basal skull fracture; in the third it was of "rheumatic" origin. In the last case paroxysmal lacrimation disappeared after a few months, whereas in the first two cases it was permanent. In all three cases shedding of tears during eating began only when the recovery of the motor paralysis was nearly complete and the previously noted ageusia entirely gone. Grobin, Altschul, Singer-Kellner and Ehlers, cited by Bing [17] (1947), observed similar cases.

Boyer and Gardner [15] reported their experience with three particularly interesting cases. The first was that of a woman operated on by Dr. W. E. Dandy for Ménière's syndrome. Immediately after the eighth cranial nerve was cut there developed paralysis of the facial nerve. It began to clear in six months and was replaced by spasm of the facial muscles. With the return of motor function excessive tearing occurred whenever she ate. Other forms of activity, including the act of chewing without food in her mouth, did not produce lacrimation. There was no demonstrable impairment of the sense of taste, but ticlike movements played about the corner of the mouth on the affected side, which showed an increase in muscular tone. Section of the greater superficial petrosal nerve abolished tearing at mealtime. One year later there was no return of the syndrome of crocodile tears. In the second case, intracranial ligation of the left middle meningeal artery and, later, section of the left greater superficial petrosal nerve were performed for intense left hemicrania. Several months after the second procedure, which at first produced some relief, the unbearable headaches recurred and were accompanied with excessive lacrimation of the left eye whenever the patient ate. No facial paralysis was present. As it was assumed that in this case the salivary nerve fibers for the parotid gland which were regenerating from the central end of the lesser superficial petrosal nerve (a branch of the glossopharyngeus), severed incidental to section of the greater superficial petrosal nerve, had become misdirected and had grown into the peripheral end of the latter, section of the ninth nerve in the posterior cranial fossa was performed. For three years, at the time of the report, the patient had been free from hemicrania and paroxysmal lacrimation. In the third case the complaints were of bouts of intense, sharp unilateral headache. With each episode of pain the left eye teared profusely and a watery secretion dripped from the left nostril. Five months after resection of the greater superficial petrosal nerve, performed for alleviation of these symptoms, hemicrania, although less severe, returned and was accompanied with a copious overflow of tears while the patient ate and with dripping of a thin, watery fluid from the left nostril. To relieve this, the

14. McGovern, F. H.: Am. J. Ophth. **23**:1388, 1940.

15. Boyer, F. C., and Gardner, W. J.: Paroxysmal Lacrimation (Syndrome of Crocodile Tears) and Its Surgical Treatment, Arch. Neurol. & Psychiat. **61**:56 (Jan.) 1949.

16. Gottesfeld, B. H., and Leavitt, F. H.: Crocodile Tears Treated by Injection into Sphenopalatine Ganglion, Arch. Neurol. & Psychiat. **47**:314 (Feb.) 1942.

17. Bing, R.: Lehrbuch der Nervenkrankheiten in 30 Vorlesungen, ed. 8, Basel, Benno Schwabe & Co., 1947.

ninth nerve was sectioned in the posterior cranial fossa, with the result that both lacrimation and nasal dripping stopped completely, although there was residual headache.

PERSONAL OBSERVATION

Mrs. W. J. (no. 1758/45), aged 36, was admitted to the neurosurgical service of the neurological clinic, University of Warsaw, on Nov. 24, 1945.

One year before, after a walk in very cold weather, the patient noticed a burning sensation in her left eye, which she could not properly close. After a few hours in a warm room the burning of the eye and the difficulty in closing it disappeared, only to return whenever the patient was exposed to cold air. It was eight months later when she was first annoyed by a certain asymmetry of the face, the angle of the mouth moving less strongly on the left side than on the right. Gradually this asymmetry of the lower part of the face grew worse, but not the difficulty in closing the eye, which was never very striking. Some nine months after the onset of her facial paresis the patient began to complain of lacrimation in the left eye whenever she took a hot soup, although she did not weep on this side when emotionally upset.

Neurological examination showed that the left side of the face was rather flat and expressionless. The left orbicularis oculi muscle was definitely weaker than the right; there was considerable difference in depth of the nasolabial folds, the left being flatter than the right, and on her showing the teeth, smiling, whistling or speaking the lips were drawn to the right side. No disturbance in the sense of taste was demonstrated. Neither the neurological nor the systemic examination revealed any other abnormality, and the usual chemical, serologic and bacteriologic examinations of the urine, blood and cerebrospinal fluid revealed nothing abnormal, except for mild anemia.

Paroxysmal lacrimation, striking and very annoying to the patient, appeared only when the patient was taking hot soup, but in no other circumstances. Galvanotherapy was advised, and the patient left the hospital on Nov. 30, 1945.

She was last seen in September 1949, almost four years after the onset of her facial paresis, when she stated that the shedding of crocodile tears had stopped several months after it had begun but that the paresis of the orbicularis oculi muscle had shown no tendency to improve. For this reason, a cervical sympathectomy was done in order to produce enophthalmos and to narrow the palpebral fissure. This operation, which was performed in another hospital, did not materially restore the symmetry of the face. Paresis of the lower branch of the left facial nerve was still present, but was very slight.

Comment.—This case, though not typical, is undoubtedly one of Bell's palsy, if this term is accepted as implying unilateral paralysis or paresis of the facial muscles which occurs as an isolated lesion without any definite etiological factor except exposure to cold (Feiling,[18] 1943). Noteworthy are the following features of this case: Although the onset of the disease was sudden, its further development was protracted, the orbicularis oculi muscle becoming weaker first and the orbicularis oris and levator labii superioris muscles much later. There was no ageusia, even in the acute stage of the paresis, but especially striking was the gradual disappearance of the syndrome of paroxysmal lacrimation, whereas paresis of the facial musculature was present four years after the onset of the disease.

Of the 18 cases of other observers in which the histories are more or less adequately reported (exclusive of the several cases of neurosyphilis and the case of vascular disease associated with subarachnoid hemorrhage recorded by Ford and Woodhall [10]), at least eight were of typical Bell's palsy. It is impossible, therefore, to accept Ford's [8] statement that the syndrome of paroxysmal lacrimation

18. Feiling, A.: Bell's Paralysis, in The British Encyclopaedia of Medical Practice Including Medicine, Surgery, Obstetrics, Gynaecology and Other Special Subjects, edited by H. Rolleston, London, Butterworth & Co., Ltd., 1936, vol. 2, p. 307.

does not occur in the common Bell's palsy. In 10 cases paralysis of the seventh cranial nerve and the syndrome of crocodile tears were caused by injury to the head or operative trauma to the nerve. It follows that in at least eight of 18 cases the nerve was not anatomically interrupted.

Boyer and Gardner's [15] two cases, in which paroxysmal lacrimation developed without previous paralysis of the facial nerve, but as a late sequel to section of the greater superficial petrosal nerve, belong, of course, to a separate group. Except for Bogorad's [5] case, in which lacrimation during eating began after complete recovery of the motor paralysis of the nerve, shedding of crocodile tears started during the motor recovery, which was then more or less advanced. In our case lacrimation during eating began about nine months after the onset of the paresis, this history being in conformity with the observations of all other authors except Kaminsky,[7] who in both his cases noted appearance of the syndrome three weeks after the beginning of the paralysis, and Christoffel,[13] whose patient shed crocodile tears from the onset of his illness.

In 10 cases "any food" (in one drinking as well) produced the unilateral tearing; in three, "appetizing" or "flavored" food; in two, only sour, salty or bitter food, and in one, sour apples and hot soup, especially (as in our own observation), and also appetizing odors and "mechanical stimulation of the inside of the mouth." Except for one patient of Savin,[11] who at the time his paroxysmal lacrimation started still had ageusia and hypesthesia, the sense of taste was normal, not tested for or not reported on.

All that is known about the extremely important question of whether the patients with crocodile tears wept emotionally on the paralyzed side as well is that Bogorad's,[5] one of Kaminsky's [7] and ours did not and that one of Ford's [8] four patients, becoming despondent, wept several times equally on the two sides.

Once the patient starts to shed his crocodile tears, he continues to do so for a long time. Exceptions to this rule are Christoffel's [13] patient, who could prevent his paroxysmal lacrimation by wearing an eyeglass during eating; Gottesfeld and Leavitt's [16] patient, whose lacrimation was stopped for a number of months by injections of alcohol into the sphenopalatine ganglion; one of Bing's,[17] whose paroxysmal lacrimation, which followed "rheumatic" facial palsy, disappeared after a few months, and all three patients of Boyer and Gardner,[15] whose crocodile tears were relieved by cutting either the greater superficial petrosal or the glossopharyngeal nerve. In our case paroxysmal lacrimation disappeared spontaneously.

In almost all the cases in which the reports were adequate the paralysis of the seventh nerve was followed by associated movements and an increase in tone of the facial musculature.

MECHANISM OF PAROXYSMAL LACRIMATION

Oppenheim [3] considered lacrimation during eating as one of the complications of paralysis of the facial nerve, since during the stage of recovery there may be associated not only the movements of the various muscles but peculiar disturbances in the sphere of taste, or the act of eating may be accompanied with that of lacrimation. Following Lipschitz [19] (1906), who explained the associated movements by misdirection of regenerating motor nerve fibers of the facial nerve, Oppen-

19. Lipschitz, R.: Monatschr. f. Psychiat. u. Neurol. **20**:84, 1906.

heim concluded that the mechanism of lacrimation during eating was of the same nature, though, as he pointed out, Micas [20] believed it to be an expression of an esophagolacrimal reflex. Later, Spiller [21] (1919) suggested that total misdirection of regenerating axons of the facial nerve may also explain the facial contracture often seen after the recovery of Bell's palsy.

To Bogorad [5] (1926) crocodile tears represented a "parareflex," caused by a merging of regenerating taste and lacrimal nerve fibers. In that concept, he followed Thomas [22] (1927), who, in explaining the pathophysiology of the auriculotemporal syndrome, expressed the thought that the pathological process and cicatrization in the auriculotemporal nerve cause the regenerating secretory nerve fibers to deviate from their normal course and grow with another neuron of different destination and physiological function. He also believed that this deviation of regenerating nerve fibers and innervation of two different tissues may form the anatomic basis of so-called axon reflexes.

Kaminsky [7] was of the opinion that the mechanism of crocodile tears is that of a pathological reflex, i. e., an accentuation of a condition potentially existing in the healthy subject, but brought to the surface by some "pathological process of very limited character." According to him, the anatomic pathway used by the gustatory impulses, arising in the taste buds of the tongue, on their way to the lacrimal gland, is as follows: The trigeminal nerve fibers from the tongue run upward with the chorda tympani, then pass the ganglion geniculi and reach the sphenopalatine ganglion and the zygomatic nerve through the greater superficial petrosal and vidian nerves. In Kaminsky's first case, in which the facial paralysis followed operative trauma to the nerve, this reflex arc, or, as he called it, "the peripheral neuron," became completely released from the control of the "central neuron." The arc becoming thus unduly excitable, the passage (in the sphenopalatine ganglion) of gustatory impulses directly into the lacrimal fibers was facilitated. The "pathological reflex" represents, therefore, a release phenomenon. However, since crocodile tears do not appear immediately after the injury, but only after a certain lapse of time, "the excitability of the secretory pathways for the lacrimal gland must be restored [beforehand]."

Ford [8] and, later, Ford and Woodhall [10] went back to the views of Lipschitz [19] to explain the syndrome of paroxysmal lacrimation by confusion of the regenerating salivary nerve fibers of the seventh nerve, some of which grow down to their proper destination, i. e., the submaxillary and sublingual ganglia, while others deviate and reach the sphenopalatine ganglion via the greater superficial petrosal and vidian nerves. Thus, through deviation of some of the salivary nerve fibers from their normal course, the patient lacrimates whenever a gustatory stimulus, calling forth salivation, is evoked.

In support of their hypothesis, they invoked the observations of Langley and Anderson [23] (1904) and Kilvington [24] (1905), who, by mechanical and electrical stimulation of motor nerves which had regenerated after being severed and had

20. Micas, cited by Oppenheim.[3]

21. Spiller, W. G.: Contracture Occurring in Partial Recovery from Paralysis of Facial Nerve and Other Nerves, Arch. Neurol. & Psychiat. **1**:564 (May) 1919.

22. Thomas, A.: Rev. neurol. **1**:447, 1927.

23. Langley, J. N., and Anderson, H. K.: J. Physiol. **31**:365, 1904.

24. Kilvington, B.: Brit. M. J. **1**:935, 1905.

reanastomosed in various combinations, showed branching of axons. Raymón y Cajal's [25] (1928) histological studies also demonstrated that the regenerating axons of peripheral nerves, previously severed, are often greatly distorted and branch profusely in the neighborhood of the injury. In the case of the facial nerve a similar state was noted by Howe and associates [26] (1937), who explained the associated movements, more apparent during strong facial innervation, and the contracture of the facial musculature in the following way:

> Either nerve fibers, totally misdirected in regeneration, may come to supply muscles with which no original connection existed, or, by branching, one regenerated axis-cylinder may innervate a large portion of the facial field.

Since their histological studies demonstrated actually branching of regenerating axons, they pointed out that the second mechanism is more likely the true one.

> Since nerve fibers conduct equally well in both directions, excitation set up at any point in an axon will be propagated throughout its entire extent. Thus, impulses initiated in motor fibers in the central stump [of one branch] would be conducted centrally, but at points of branching . . . would also pass distally in [another] branch.

In fact, by stimulating one of the facial muscles in their experimental animals, they could produce contraction of other muscles, even if the facial nerve has been severed from the pons; that is, the possibility of a reflex response to stimulation of sensory fibers in the facial nerve was eliminated. They believed, then, that in the early stages of regeneration and dysfunction the misdirected fibers may play a contributory role in the mechanism of associated movements, but that as these movements, once established, do not as a rule become suppressed, modified or eliminated by reeducation, they are due chiefly to the presence of bifurcated axons.

Bing [27] (1939, 1947), stating that his experience with lacrimation accompanying eating dated from 1924, expressed the opinion that this phenomenon is due to a gustolacrimal reflex, which is a release phenomenon, like other pathological reflexes, such as the Babinski sign, and is caused by functional interruption of the nerve fibers of the facial nerve somewhere between the ganglion geniculi and the chorda tympani. This "reflex" appears only after complete recovery of the sense of taste, but before that of the motor function of the nerve. His ideas concerning the anatomy and physiology of the fifth and seventh cranial nerves, upheld even in the 1947 edition of his "Lehrbuch der Nervenkrankheiten," are contrary to everything known to date about the embryology, anatomy and physiology of those two nerves and recall the notions of bygone days.

Tumarkin,[9] Russin,[12] Savin [11] and Boyer and Gardner [15] all interpreted the syndrome of paroxysmal lacrimation as a phenomenon caused by misdirection of regenerating salivary nerve fibers, some of which, formerly supplying the salivary glands, come to innervate the lacrimal gland as well.

In the two cases of paroxysmal lacrimation (Boyer and Gardner [15]) which developed without previous paralysis of the seventh nerve, but as a sequel to section

25. Raymón y Cajal, S.: Degeneration and Regeneration of the Nervous System, translated and edited by R. M. May, New York, Oxford University Press, 1928.

26. Howe, H. A.; Tower, S. S., and Duel, A. B.: Facial Tic in Relation to Injury of Facial Nerve: Experimental Study, Arch. Neurol. & Psychiat. **38**:1190 (Dec.) 1937.

27. Bing, R.: Schweiz. med. Wchnschr. **69**:36, 1939; footnote 17.

of the greater superficial petrosal nerve for hemicrania, the syndrome was, according to these authors, due to misdirection of salivary fibers—however, not of the facial, but of the glossopharyngeal, nerve. The lesser superficial petrosal nerve, a branch of the latter, carrying salivary fibers for the parotid gland, runs in the middle cranial fossa parallel to the greater superficial petrosal nerve, just a few millimeters anterior to it. Therefore, any resection of the latter includes the severance of the former. As section of the ninth nerve in the posterior cranial fossa relieved this condition, in which gustatory stimuli evoked lacrimation, it was assumed that the regenerating salivary fibers of the lesser superficial petrosal nerve must have formed connection with the lacrimal gland through the distal end of the greater superficial petrosal nerve. Indeed, Boyer and Gardner [15] believed that "the surgical relief obtained in these cases furnishes proof for the theory that the syndrome is caused by misdirection of regenerating salivary fibers."

That any dysfunction of lacrimation associated with Bell's palsy must, as a rule, be due to a lesion of the nerve situated central to or at the level of the issue of the greater superficial petrosal nerve is obvious, in view of what is known of the anatomy and physiology of lacrimation.

As could be seen from the recorded case histories, in almost half the patients the damage done to the facial nerve surely did not even approach that of complete anatomic interruption, being probably of the nature of interstitial neuritis, which leaves the intrinsic pattern of the nerve intact. It is true that even with such a lesion regenerating axons do branch and may deviate from their normal course, since in such an injury, which disrupts the endoneurial tubes, regenerating axis-cylinders from the portion of the nerve central to the lesion must compete for the available endoneurial tubes in the peripheral stump. Indeed, there is no mechanism which insures that each axon will reenter its corresponding endoneurial tube and thereby fully reconstitute the fiber pattern (Sunderland and Bedbrook,[28] 1949). But since the lesion of the facial nerve causing the syndrome of paroxysmal lacrimation must always be located central to or at the level of the issue of the greater superficial petrosal nerve, i. e., in that portion of the seventh cranial nerve in which, as will be shown later, there is a relatively high degree of localization of fibers representing its individual branches, the chances of reestablishing old connections by regenerating axons are favorable (Sunderland,[29] 1945). On the other hand, the regenerating axons of the salivary nerve fibers (damaged somewhere central to the exit of the greater superficial petrosal nerve), to be able to cause lacrimation simultaneous with salivation, would have to produce collaterals of quite a length, which, being partly misdirected, would have to travel far. Before they eventually could reach the sphenopalatine ganglion, and thence the lacrimal gland, they would encounter on their way, through the greater superficial petrosal and vidian nerves, the products of degeneration of both the medullated and the unmedullated efferent fibers of these nerves, their undegenerated afferent fibers and the undegenerated sympathetic fibers of the lateral ramus of the internal carotid nerve, which join the greater superficial petrosal nerve in the so-called greater deep petrosal nerve.

28. Sunderland, S., and Bedbrook, G. M.: Brain **72**:613, 1949.

29. Sunderland, S.: Brain **68**:243, 1945.

Is one to assume that not all the nerve fibers injured in a case of Bell's palsy recover their function, although some do so more slowly and perhaps not always completely, but believe that it is only the lacrimal fibers which do not regenerate, whereas the others, such as the motor and taste sensory fibers, usually do, and those destined for the salivary glands even show the peculiar tendency to branch, deviate and synapse with nerve cells to which they do not belong? In doing so, one would be forced to accept this extraordinary abnegation of the lacrimal fibers and, at the same time, the unusual dynamism of the salivary fibers, even in the two cases of Boyer and Gardner,[15] in which there was no injury of the facial nerve and in which it was assumed that it was the salivary fibers of the lesser superficial petrosal nerve, i. e., the glossopharyngeal nerve, which found their way to the sphenopalatine ganglion via the vidian nerve.

Theoretically, it is conceivable that branching axons of the regenerating salivary fibers of the facial nerve could ultimately reach both the salivary and the lacrimal glands and thus cause lacrimation during salivation. Practically, however, is it likely to happen? That the regenerating axons of the previously injured nerve trunk do branch in the neighborhood of the injury is a fact, the accuracy of which is beyond discussion. But, distortion and branching of the axons at or near the site of a nerve lesion is one thing, and sprouting of collaterals, which must then deviate from the normal course of their parent nerve trunk and travel a long way, finally to synapse with nerve cells of an alien ganglion, is quite another. Attractive as this hypothesis may be, it is by no means proved. Therefore, before accepting this explanation, one should exclude the possibility of some other nerve pathway being used for eliciting this undoubtedly reflex phenomenon. One of these may be represented by the sympathetic root of the sphenopalatine ganglion, i. e., the greater deep petrosal nerve.

It is surprising how little is known about the functional significance of this sympathetic component of the sphenopalatine ganglion, and, consequently the innervation of the lacrimal gland by the sympathetic nervous system, although as early as 1891 Arloing [30] suggested that the lacrimal gland is supplied by fibers originating in the cervical sympathetic trunk. He assumed that their function is inhibitory. Brüning [31] (1923) and Köhler and Weth [32] (1923), but chiefly Müller [33] (1924), comparing the secretory activity of the lacrimal gland with that of the salivary glands, expressed the opinion that the excessive lacrimation observed the first few days after section of the cervical sympathetic nerve, the function of which they thought was inhibitory, is best explained by the then unrestricted secretory activity of the parasympathetic nervous system. However, accepting this analogy, one would rather expect the cervical sympathetic nerve to carry to the lacrimal glands actively secretory fibers, it being known since Ludwig's [34] (1856) original work that the salivary glands do receive such fibers. In fact, as a result of

30. Arloing, G.: Arch. de physiol. norm. et path. **3**:241, 1891.

31. Brüning, F., and Stahl, O.: Die Chirurgie des vegetativen Nervensystems, Berlin, Springer-Verlag, 1924.

32. Köhler and Weth, cited by Hesse, E.: Die Chirurgie des vegetativen Nervensystems, Moscow and Leningrad, Staatsverlag, 1930.

33. Müller, L. R.: Die Lebensnerven, Berlin, Springer-Verlag, 1924.

34. Ludwig, C., cited by Langley, J. N.: The Salivary Glands, in Schäfer, E. A.: Text-Book of Physiology, London, Y. J. Pentland, 1898.

Claude Bernard's [35] (1858) and Eckhard's [36] (1863) experiments, it is known that stimulation of the sympathetic fibers produces saliva which is different from that obtained on stimulation of the chorda tympani, it being viscid and containing a higher percentage of solids. The secretory innervation of the salivary glands by sympathetic fibers was confirmed by Stavraky [37] (1931). Réthi [38] (1904) showed the same thing with respect to the glands of the mucous membrane of the soft palate, which are principally innervated by the parasympathetic fibers of the facial nerve. Indeed, Hesse [39] (1930) mentioned that epiphora follows stimulation of the cervical sympathetic trunk.

It is conceivable, therefore, that the tears seen in patients with the syndrome of paroxysmal lacrimation are the result of sympathetic, rather than parasympathetic, stimulation, the efferent impulses being transmitted from the central nervous system to the sphenopalatine ganglion by the internal carotid, the greater superficial petrosal and the vidian nerves. Relief of crocodile tears by unilateral resection of the superior cervical sympathetic ganglion would confirm this possibility, remote as it is, whereas absence of improvement would disprove it.

Vulpian and Journiac [40] (1879), stimulating the nerves of the tympanic cavity in rabbits, noted among other effects, lacrimation and secretion from the harderian gland. After section of the facial nerve, stimulation of the tympanic nerves produced only slight tearing and no secretion from the harderian gland. As the tympanic plexus is built up of two components, namely, a sympathetic and a parasympathetic one, the latter belonging to the glossopharyngeal nerve, it is, of course, difficult to be sure which one of these two components of the tympanic plexus was actually responsible for the observed lacrimation. It might be the sympathetic; it might be the parasympathetic, represented by its glossopharyngeal outflow.

Indeed, it seems to have been overlooked that as early as 1842 Bidder [41] described a connection between the otic ganglion and the vidian nerve "having the appearance of a sympathetic nerve." A similar anastomosis, but between the otic ganglion and the greater superficial petrosal nerve, was noted by Krause [42] (1848), who called it the nervulus sphenoidalis internus, in contradistinction to the nervulus sphenoidalis externus, which links the otic with the gasserian ganglion. Rauber [43] (1872) observed that this "nervulus," before it reaches the foramen lacerum and the vidian nerve divides into two branches, the one running with the latter toward the sphenopalatine ganglion, while the other, turning backward, follows the greater superficial petrosal nerve toward the ganglion geniculi

35. Bernard, C.: Leçons sur la physiologie et la pathologie du système nerveux, Paris, J. B. Baillière et fils, 1858.

36. Eckhard: Beitr. z. Anat. u. Physiol. **3**:125, 1863.

37. Stravraky, G. W.: Quart. J. Exper. Physiol. **21**:123, 1931.

38. Réthi, L.: Wien. med. Presse **45**:213, 1904.

39. Hesse, E.: Die Chirurgie des vegetativen Nervensystems, Moscow and Leningrad, Staatsverlag, 1930.

40. Vulpian and Journiac: Compt. rend. Acad. d. sc. **89**:393, 1879.

41. Bidder, F. H.: Die Selbständigkeit des sympathischen Nervensystems, Leipzig, Breitkopf und Hartel, 1842.

42. Krause, C., cited by Rauber, A. A.: Über den sympathischen Grenzstrang des menschlichen Kopfes, Munich, J. J. Lentner, 1872.

43. Rauber, A. A.: Über den sympathischen Grenzstrang des menschlichen Kopfes, Munich, J. J. Lentner, 1872.

(fig. 1). At the site of entry of the nervulus sphenoidalis internus into the vidian nerve, the presence of a small ganglion was demonstrated by Rauber [43] (1872) three times in six dissections. Rauber and Kopsch [44] (1909) confirmed the anastomosis described above.

There is still another pathway through which the impulses initiated by the parasympathetic nervous system could reach, via the glossopharyngeal outflow, the sphenopalatine ganglion and the lacrimal gland, namely, the ramus communicans cum plexu tympanico of Pieschel [45] (1844), Arnold [46] (1851) and Henle [47] (1868).

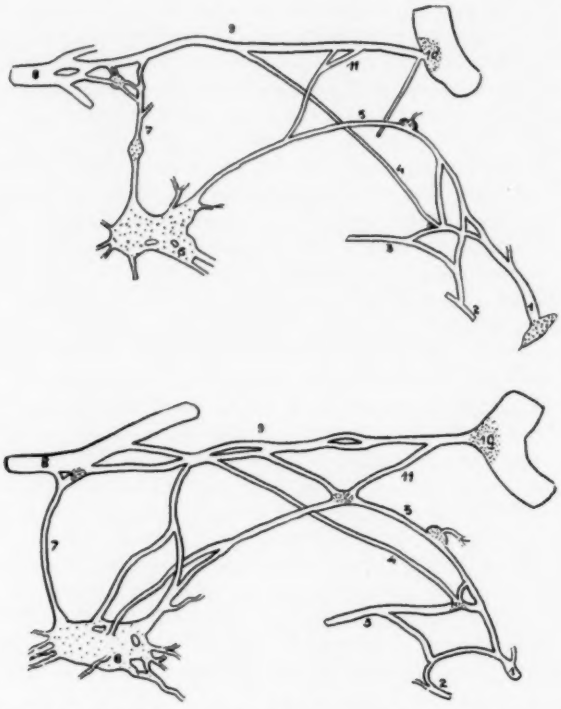

Fig. 1.—Rauber's [43] plate III, figures 1 and 2 (redrawn): *1*, indicates nervus tympanicus; *2*, nervus caroticotympanicus; *3*, nervus tubae Eustachii; *4*, nervus tympanicocaroticus seu nervus petrosus profundus minor; *5*, nervus petrosus superficialis minor; *6*, ganglion oticum; *7*, nervus sphenoidalis internus; *8*, nervus vidianus; *9*, nervus petrosus superficialis major; *10*, ganglion geniculi; *11*, anastomosis between nervus petrosus superficialis major and nervus superficialis minor.

44. Rauber, A. A., and Kopsch: Lehrbuch der Anatomie des Menschen, ed. 8, Leipzig, G. Thieme, 1909.

45. Pieschel, C. A., cited by Arnold, F.: Handbuch der Anatomie der Nerven des Menschen, Freiburg, Herder, 1851.

46. Arnold, F.: Handbuch der Anatomie der Nerven des Menschen, Freiburg, Herder, 1851.

47. Henle, F. G. J.: Handbuch der systematischen Anatomie des Menschen, Braunschweig, F. Vieweg u. Sohn, 1856-1873.

It links the tympanic plexus or the otic ganglion with the greater superficial petrosal nerve. In fact, the tympanic nerve forms connections between four ganglia (fig. 2); starting with the ganglion petrosum, of the ninth nerve, it runs forward and sends branches to the ganglion geniculi and to the ganglion oticum and ganglion sphenopalatinum. The relations of this nerve, which are so complex in mammals, become especially so in man (Wilder,[48] 1923).

In short, there are at least two paths through which efferent impulses passing through the glossopharyngeal nerve could reach the sphenopalatine ganglion and the lacrimal gland—the nervulus sphenoidalis internus and the ramus communicans (of the greater superficial petrosal nerve) cum plexu tympanico. It is true that nothing is known of either the histological nature or the functional significance of those two nerves, but the relief of paroxysmal lacrimation obtained by Boyer and Gardner [15] by section of the ninth nerve suggests that at least the nervulus sphenoidalis internus may actually carry secretory nerve fibers for the lacrimal gland.

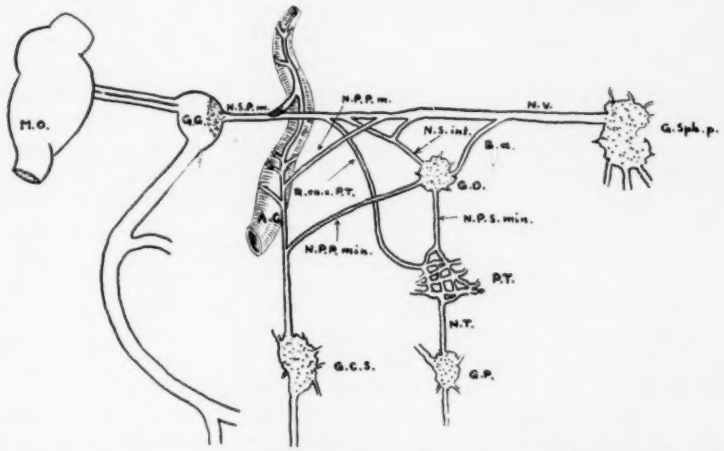

Fig. 2.—Schema showing the connections between the parasympathetic outflow of the facial and glossopharyngeal nerves. *M.O.* is the medulla oblongata; *G.G.*, ganglion geniculi; *N.S.P.m.*, nervus petrosus superficialis major; *A.C.*, internal carotid artery; *G.C.S.*, superior cervical ganglion; *N.P.P.min.*, nervus petrosus profundus minor; *R.co.c.P.T.*, ramus communicans cum plexu tympanico; *N.P.P.m.*, nervus petrosus profundus major; *N.S.int.*, nervulus sphenoidalis internus; *G.O.*, ganglion oticum; *N.P.S.min.*, nervus petrosus superficialis minor; *P.T.*, plexus tympanicus; *N.T.*, nervus tympanicus (nervus Jacobsoni); *G.P.*, ganglion petrosum; *B.a.*, Bidder's anastomosis; *N.V.*, nervus vidianus, *G.Sph.p.*, ganglion sphenopalatinum.

Since this anastomosis, linking the glossopharyngeal with the vidian nerve, was not necessarily injured incidental to resection of the greater superficial petrosal nerve for hemicrania, it could well be responsible for the observed lacrimation during eating. It may be of interest to add that Landolt [49] (1903), who was the first to demonstrate the innervation of the lacrimal gland by fibers running in the greater superficial petrosal and vidian nerves, raised the question whether these lacrimal fibers of the branches of the facial nerve do not actually reach them from the glossopharyngeal nerve.

48. Wilder, H. H.: The History of the Human Body, ed. 2, New York, Henry Holt & Company, 1923.

49. Landolt, H.: Arch. f. d. ges. Physiol. **98**:189, 1903.

The striking fact that many a patient with the syndrome of paroxysmal lacrimation does not weep spontaneously, on emotional provocation, speaks strongly for the assumption that it is another nerve than the facial which incites the lacrimal gland to secrete in these circumstances. The sympathetic, especially the glossopharyngeal, nerve would be the logical suggestion, inasmuch as this double innervation of one and the same organ by those two cranial nerves is already represented in the joint sensory innervation of the tongue. Yet why should this nerve, unaffected, as it is, in the case of Bell's palsy, behave so strangely as to cause this weeping when the patient eats, and then not at once, but only at a certain time after the onset of paralysis of the seventh nerve?

Is there no other way, therefore, of explaining the phenomenon of paroxysmal lacrimation?

It will be recalled that 10 to 14 weeks after section the regenerating nerves show an increased excitability which, according to Trotter and Davies [50] (1913, 1926), is caused by imperfect insulation of their axis-cylinders: When the normal insulation of nerve fibers by the neurilemma sheaths is broken down, there is an extravagant proliferation of axons, which are then subjected to constant subliminal stimuli and placed in a state of increased excitability. The neighboring axons, lacking their insulation, may fuse. Speidel [51] (1935), Young [52] (1944) and Katz and Schmitt [53] (1940) have shown that in certain conditions efferent nerve impulses can alter the excitability of adjacent sensory nerve fibers; that is, the adjacent nerve fibers may interact. This has already been demonstrated by Adrian [54] (1930). In the light of these observations, Doupe and associates [55] (1944) drew attention to the possibility that the peculiar quality of causalgic pain is due to activation of sensory fibers by adjacent sympathetic vasomotor, pilomotor and sudomotor fibers, this cross stimulation occurring through defective insulation of axons. This interesting hypothesis, furnishing, as pointed out by White [56] (1946), an explanation for the increase of causalgic pain during any form of emotional excitement, cutaneous stimulation or everyday visual and auditory stimulation, has been given direct experimental proof by Granit and associates [57] (1944). They actually demonstrated in cats cross stimulation between motor and sensory fibers and vice versa, at the point of injury to the sciatic nerve, which consisted in its section, or even ligation. They recorded with the cathode ray oscillograph an afferent discharge from the spinal sensory root when the motor root was stimulated, as well as reverse, and concluded that the small, poorly myelinated axons of the group of C fibers are especially susceptible to "fiber interaction."

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50. Trotter, W.: Brit. M. J. **2**:107, 1926. Trotter, W., and Davies, H. M.: J. f. Psychol. u. Neurol. **20**:102, 1913.

51. Speidel, C. C.: J. Comp. Neurol. **61**:1, 1935.

52. Young, cited by Doupe, J.; Cullen, C. H., and Chance, G. Q.: J. Neurol., Neurosurg. & Psychiat. **7**:33, 1944.

53. Katz, B., and Schmitt, O. H.: J. Physiol. **97**:471, 1940.

54. Adrian, E. D.: Proc. Roy. Soc., London, s.B **106**:596, 1930.

55. Doupe, J.; Cullen, C. H., and Chance, G. Q.: J. Neurol., Neurosurg. & Psychiat. **7**:33, 1944.

56. White, J. C.: Am. J. Surg. **72**:468, 1946.

57. Granit, R.; Leksell, L., and Skoglung, C. R.: Brain **67**:125, 1944.

The facial nerve is a complex structure,[58] being composed of several distinct fiber components, namely, the very large and the large myelinated, rapidly conducting motor and sensory A fibers; the considerably more slowly conducting, finely myelinated B fibers, largely made up of preganglionic axons, and the unmyelinated, most slowly conducting C fibers, partly afferent and partly autonomic in function.

The motor division of the seventh cranial nerve is predominantly composed of myelinated fibers of very large caliber, like those of the motor portion of the fifth nerve, then of smaller myelinated fibers, still of about 10 microns' diameter, like those of the nervus intermedius of Wrisberg,[59] and of some unmyelinated nerve fibers. The larger fibers are undoubtedly motor in function, whereas the smaller myelinated and unmyelinated fibers in part are afferent and in part belong to the parasympathetic nervous system. The lateral branches of the nerve, which here are of most interest, namely, the greater superficial petrosal and the vidian nerves, contain, as noted by Chorobski[60] (1932), among the unmyelinated and small myelinated fibers, analogous to those found in the internal carotid nerve, great numbers of large myelinated fibers, measuring about 10 microns in diameter. The latter are afferent in function, since they invariably degenerate when the greater superficial petrosal nerve is cut distal to the ganglion geniculi. Some of the small myelinated nerve fibers of the greater superficial petrosal nerve arise in the superior cervical sympathetic ganglion, as they degenerate after it has been excised, while others of the same caliber, which can be traced from the nervus intermedius directly into the greater superficial petrosal nerve, running in closely packed fasciculi, degenerate after the facial nerve has been severed near the brain stem.

Almost all the nerve fibers of the six afferent components of the facial nerve, which have their cells of origin in the geniculate ganglion, run toward the central nervous system in the nervus intermedius (nervus Wrisbergi). Whether all the parasympathetic nerve fibers of the facial nerve run between the brain stem and the genu of the nerve in its sensory root is not entirely settled. In Macacus rhesus monkeys each root of the seventh nerve seems to carry nerve fibers proper to both, though the motor portion in these animals is entirely separated from the sensory (Chorobski,[60] 1932). Section of the seventh nerve near the brain stem causes degeneration not only of the very large myelinated fibers of the motor division but of the small myelinated and unmyelinated fibers, of small and medium diameter, in the nervus intermedius. Incidentally, destruction of the geniculate ganglion is followed by degeneration not only of all the large myelinated fibers of the nervus intermedius but also of some of the large myelinated and unmyelinated nerve fibers of the motor portion.

58. The rather complex anatomy and physiology of the facial nerve is dealt with in the majority of even the most recent textbooks on neuroanatomy, both descriptive and "functional," the textbooks or monographs on neurophysiology, etc., in a singularly simplified way. Their authors seem not only to ignore the newer contributions to the subject, some of which have found confirmation by independent observers, but also to overlook many of the earlier findings, which, so far as it is known, have been disproved by no one.

59. My whole experience with the morphology of the seventh nerve and its branches was gained while working in Dr. Wilder Penfield's Laboratory of Neuropathology, McGill University, from 1930 to 1932.

60. Chorobski, J.: A Vasodilator Nervous Pathway to the Cerebral Blood Vessels from the Central Nervous System, and on the Occurrence of Afferent Nerve Fibres in the Internal Carotid Plexus, Thesis, McGill University, Montreal, Canada, 1932.

In the 12 week human embryo, as shown by His [61] (1889), there is no such structure as a separate nervus intermedius, its fibers running partly with the acoustic and partly with the facial nerve. This strongly suggests that the differentiation of the seventh nerve, which takes place later, may seldom, if ever, become complete. However, in adult man, Tarlov [62] (1937) demonstrated that the nervus intermedius is morphologically quite different from the motor portion of the nerve and that its attachment to the brain stem is composed of two roots, presenting the contrasting features of the anterior and the posterior spinal roots. The gross and microscopic features of these two types of roots suggest a separation of the nervus intermedius into sensory (larger) and motor (smaller) components. The latter may in some cases undergo further division into separate rootlets, containing nerve fibers of probably different function, i. e., vasodilatation and glandular secretion. Nevertheless, as varying degrees of approximation, and even fusion, of the rootlets of the nervus intermedius may occur, it is safer to assume that the general visceral efferent fibers of the facial nerve are contained in both its divisions, although their principal outlet is in the nervus intermedius (nervus Wrisbergi).

It is well known, of course, that nerve fibers cut off from their cells of origin do not degenerate simultaneously but may show in a given period of study all stages of degeneration and regeneration. In the case of the seventh nerve, Howe and associates [26] showed that three months after section, hemisection or even freezing of the nerve the regenerating axons of the myelinated nerve fibers vary extremely in size and degree of myelination. Seddon [63] (1942, 1944), reviewing the problem of peripheral nerve injuries, concluded that the chief characteristic of their more or less transient block, produced by an injury which does not actually sever the nerve, is that the vulnerability of its various fibers is approximately a function of their size. The larger the fiber, the slower the recovery, and presumably the greater the intensity of the damage. Indeed, Köster [1] found that among the fibers composing the facial nerve the most vulnerable seem to be the motor, since the first to recover are usually the taste fibers, then the secretory fibers for the salivary glands, then the lacrimal fibers and finally the motor fibers.

In summary, in many cases of facial nerve paralysis, complicated by the syndrome of paroxysmal lacrimation, the condition is most probably caused by an inflammatory swelling of the nerve, which, since the rigid walls of the facial canal (Fallopian aqueduct) limit its expansion, becomes compressed. The resulting lesion in continuity, responsible for the paralysis, is characterized by the breakdown of the nerve fibers, with the survival of the connective tissue of the nerve, which facilitates the often observed spontaneous regeneration of the nerve. The facial nerve being a mixed one, its recovery seemingly follows the rule that the vulnerability of the fibers of such a nerve is approximately a function of their size. The salivary and the lacrimal nerve fibers recover later than the taste fibers, but before the motor fibers, and are finely myelinated and unmyelinated. Both sets of nerve fibers run chiefly in adjacent fasciculi, and so their inadequate insulation

61. His, W.: Arch. f. Anat. u. Physiol. 1889, supp. C, p. 1.

62. Tarlov, I. M.: Structure of Nerve Root: Differentiation of Sensory from Motor Roots; Observations on Identification of Function in Roots of Mixed Cranial Nerves, Arch. Neurol. & Psychiat. **37**:1338 (June) 1937.

63. Seddon, H. J.: Brit. M. J. **2**:237, 1942; Brain **66**:237, 1944.

during recovery of the nerve may well cause their interaction. The functional and perhaps anatomic fusion of the motor nerve fibers, destined for the various facial muscles, could explain the mechanism of the mass movements and the facial contracture, while interaction between the adjacent autonomic and taste fibers of the facial nerve may account for the phenomenon of unilateral lacrimation whenever the patient eats certain foods.

Of course, such a fiber interaction is not necessarily limited to the lacrimal and salivary fibers destined for the submaxillary and sublingual glands; it may occur as well between the lacrimal and the secretory nerve fibers destined for the glands of the mucous membrane of the soft palate and nasal cavity. The demonstration by Prevost [64] (1868) that stimulation of the sphenopalatine ganglion produces an abundant secretion of a transparent serous fluid from the nose was confirmed by Aschenbrandt [65] (1885), who pointed out that this secretion is similar in its microscopic appearance to the saliva obtained from the submaxillary gland, and later by Réthi [28] (1904) and Jung and associates [66] (1927).

As a matter of fact, the cross stimulation in the injured facial nerve may occur not only between the lacrimal and the salivary fibers of whatever destination but between all the other autonomic nerve fibers of the nerve as well, running, as they do, central to its genu and in the greater superficial petrosal nerve in close proximity. It fact, there is no reason at all to suppose that it is only the salivary discharge, evoked by gustatory stimuli, which can cause a simultaneous effect in two different tissues. If, however, one does not observe in cases of Bell's palsy a syndrome of paroxysmal salivation or paroxysmal vasodilatation, the reason is surely that unilateral secretion of saliva or unilateral vasodilatation in the mucous membrane of the soft palate or the pial blood vessels during weeping is obviously less conspicuous than lacrimation during eating. Of course, this reasoning could also apply to the hypothesis postulating deviation of the collaterals of regenerating nerve fibers, since it is hardly conceivable that it is only the salivary fibers which, after being injured, branch and innervate tissues for which they were not destined.

In a case of Bell's palsy without ageusia the gustatory stimuli necessary to evoke the crocodile tears may easily be transmitted to the central nervous system through the taste fibers of both the facial and the glossopharyngeal nerve. Indeed, both nerves must usually carry them, as the tongue is not equally sensitive at all points to all primitive taste sensations, the back reacting more easily to bitter stimuli and the tip and the sides to sweet and sour substances (Starling,[67] 1920), and as the patient is commonly stimulated to weep by more than one of these sensations. It is known also that the various taste sensations are served by different nerve endings, since under certain conditions the bitter sensation disappears first, then the sweet and then the sour, whereas the salty taste appears to remain unaffected. This topographic and functional specificity of the endings of the taste fibers would account for the variation from case to case in the nature of the gustatory stimulation which is likely to elicit the crocodile tears and for its appearance in several different combinations in each case. Therefore, in a patient

64. Prevost, J. L.: Arch. de physiol. norm et path. **1**:7 and 207, 1868.

65. Aschenbrandt: Monatsschr. f. Ohrenh. **19**:65, 1885.

66. Jung, L.; Tagand, R., and Chavanne, F.: Arch. internat. de laryng. **6**:54, 1927.

67. Starling, E.: Principles of Human Physiology, ed. 3, London, J. A. Churchill, 1920.

with Bell's palsy who lacrimates whenever he eats sweet or sour substances, but who presents a disturbance in the sense of taste over the anterior two thirds of the tongue, the sensations must originate in taste buds located elsewhere than in the tongue and be conveyed to the central nervous system by some way other than that of the glossopharyngeal nerve.

As shown above, the vidian and the greater superficial petrosal nerve carry a certian number of afferent nerve fibers, the majority of which are destined for the mucous membrane of the nose and the soft palate. They pass uninterrupted through the sphenopalatine ganglion; enter at least some of its branches and degenerate only when cut off from the geniculate ganglion (Chorobski and Penfield,[68] 1932). Some of those afferent nerve fibers supply taste buds of the

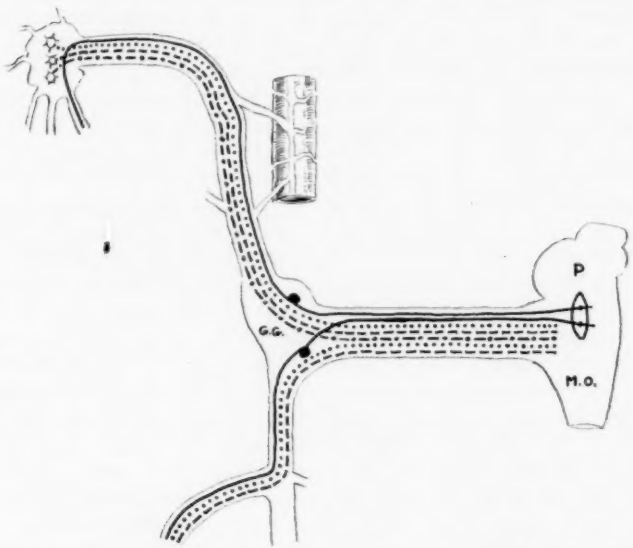

Fig. 3.—Schema of the fibers of the facial nerve, chorda tympani and greater superficial petrosal nerve, interaction of which may cause lacrimation simultaneous with salivation (gustatory stimulus).

soft palate, as pointed out by Dixon[69] (1899) and later by Cushing[70] (1903). A gustatory stimulus evoked in the taste buds located here, and carried toward the central nervous system by the afferent fibers of the vidian and greater superficial petrosal nerves, could well cross stimulate the lacrimal nerve fibers lacking, at the site of nerve injury or peripheral to it, adequate insulation, there being no reason that only an efferent nerve impulse could, at the point of a nerve lesion, cross to the afferent fibers and not vice versa (fig. 3).

68. Chorobski, J., and Penfield, W.: Cerebral Vasodilator Nerves and Their Pathway from Medulla Oblongata, Arch. Neurol. & Psychiat. **28**:1257 (Dec.) 1932.

69. Dixon, A. F.: J. Anat. & Physiol. **33**:471, 1899.

70. Cushing, H.: Bull. Johns Hopkins Hosp. **14**:71, 1903.

Uprus and associates [71] (1934), discussing their case of abnormal flushing and sweating during eating, a condition undoubtedly allied to paroxysmal lacrimation, expressed the opinion that "the period of latency between the original trauma and onset of symptoms is consistent with an unusual regenerative phenomenon having occurred," favoring, in their case, the interference of branched axons. It seems however, that the emphasis placed on the "unusual regenerative phenomenon" might apply to the fiber interaction as well, since here, too, a delay is necessary for the axons to lose their insulation and be ready to interact. The disturbance in myelination in the injured axons of the facial nerve is apparently protracted, since the syndrome of paroxysmal lacrimation, once established, lasts usually for months, if not years. However, this is not always so, as can be seen from one of Bing's [17] cases, in which the crocodile tears, which followed "rheumatic" facial palsy, disappeared after a few months, as well as from the present case. How this spontaneous recovery is brought about is uncertain, but ultimate remyelination of the previously naked axons seems to be the answer. Echlin and associates [72] (1949) believed that the gradual improvement in many cases of causalgic pain, for which they accept the mechanism of cross stimulation between afferent and efferent nerve fibers, is due to the setting up of an inflammatory reaction and interstitial fibrosis at the site of injury, ultimately separating or insulating the interacting fibers.

The discrepancy between the faculty of shedding tears on gustatory stimulation and, at the same time, the absence of spontaneous lacrimation in patients with the syndrome of crocodile tears is admittedly the stumbling block for all the theories of their mechanism. However, accepting the hypothesis proposed in this paper, could one not explain this phenomenon by a summation of successive gustatory stimuli, which exciting, as they usually do, the taste fibers of both the facial and the glossopharyngeal nerves, and playing on the same reflex center, are thus sufficiently strong to produce discharges in the facial salivary fibers and cross stimulate the lacrimal fibers, whereas an emotional stimulus fails to produce a discharge in these, still not normally functioning, nerve fibers?

On the assumption that acetylcholine liberated in the tissues causes contraction of skeletal muscle fibers which have been rendered chemically hypersensitive by degeneration of their motor nerves, Lewy and associates [73] (1937, 1938) concluded that the paroxysmal lacrimation might be accounted for on the basis of injury to the lacrimal fibers in the chorda tympani (!) and the resultant sensitization of the lacrimal gland to the diffuse liberation of acetylcholine which occurs during mastication. This hypothesis, which they applied to similar phenomena, with reference to which it seems to have been disproved by Corbin and associates [74] (1941), is untenable with respect to crocodile tears, since this condition is almost never observed after the simple act of mastication. It is not chewing which causes the patient to weep while eating, but certain gustatory sensations, which vary from one case to another.

71. Uprus, V.; Gaylor, J. B., and Carmichael, E. A.: Brain **57**:443, 1934.

72. Echlin, F.; Owens, F. M., and Wells, W. L.: Observations on "Major" and "Minor" Causalgia, Arch. Neurol. & Psychiat. **62**:183 (Aug.) 1949.

73. Lewy, F. H.; Groff, R. A., and Grant, F. C.: Autonomic Innervation of the Eyelids and the Marcus Gunn Phenomenon, Arch. Neurol. & Psychiat. **37**:1289 (June) 1937; Autonomic Innervation of the Face: II. An Experimental Study, ibid. **39**:1238 (June) 1938.

74. Corbin, K. B.; Harrison, F., and Wigginton, C.: Elicitation of the "Pseudomotor Contracture" in the Tongue by Intramedullary Stimulation, Arch. Neurol. & Psychiat. **45**:271 (Feb.) 1941.

Undoubtedly, my explanation of the mechanism of crocodile tears is a hypothesis only, lacking direct proof; but, as already pointed out, so is the attempt to explain them by misdirection of the regenerating axons of the salivary nerve fibers. The premises of both conceptions are based on proved facts—in the first case on fiber interaction and in the second on branching of the regenerating axons at the site of nerve injury. Therefore, the choice between the two should be made dependent on which explains most of the features of the phenomenon. My view seems to explain the mechanism of paroxysmal lacrimation somewhat better than others.[75]

Indeed, "there are no paradoxes in the organism, and whenever they seemingly occur they cover some still unknown principle of a general nature" (Heidenhain,[76] 1883).

SUMMARY

A case of facial paresis of protracted development, complicated by the syndrome of crocodile tears, or paroxysmal lacrimation, is reported. Tearing whenever the patient took hot soup appeared several months after the onset of the disease and then disappeared spontaneously, though she never fully recovered from the motor paresis.

A review of the literature concerned with paroxysmal lacrimation shows that this phenomenon may follow paralysis of the facial nerve of whatever cause; that it may appear right at the onset of the disease or, more frequently, after a certain period, either as the only sequel of the nerve lesion or in association with such disturbances as "tic," increased tone of the facial musculature, or ageusia; that this shedding of tears during eating lasts usually for months or years but may be of shorter duration; that it is produced by the primitive sensations of taste, singly or in various combinations, and practically never by other agents, such as mechanical stimulation or chewing without food.

Almost all the patients known to have been affected by lacrimation during eating did not weep spontaneously on emotional stimulation.

The now almost universally accepted hypothesis explaining the paroxysmal lacrimation by misdirection of some of the collaterals of regenerating axons of salivary nerve fibers, innervating thus both the salivary and the lacrimal glands, is discussed. In lieu of this proposed explanation, which, although attractive, is not entirely satisfactory, another is offered, based on the concept of cross stimulation, which, as has been shown in other circumstances, does occur between various fiber components of a nerve at the site of its injury. The short-circuiting of nerve impulses may take place between the inadequately insulated autonomic components of the facial nerve or between these and the afferent nerve fibers, as a nerve impulse "does not vary in essentials" "whether set up by end organs or nerve stimulation, and whether subserving motor or sensory function" (Walshe,[77] 1948).

75. Should this hypothesis be found valid, one would be tempted to apply this hypothesis to some undoubtedly allied conditions, such as the auriculotemporal syndrome of Frey (Rev. Neurol. **2**:97, 1923), and, in the realm of disturbances in the central nervous system, to the curious *décharges électriques* of Lhermitte (Multiple Sclerosis: The Sensation of an Electrical Discharge as an Early Symptom, Arch. Neurol. & Psychiat. **22**:5 [July] 1929), observed in multiple sclerosis, in which demyelination of relatively intact axons represents, of course, the fundamental pathologic process.

76. Heidenhain, R.: Über pseudomotorische Nervenwirkungen, Arch. f. Physiol., 1883, supp. p. 133-177.

77. Walshe, F. M. R.: Critical Study in Neurology, Edinburgh, E. & S. Livingstone, 1948.

PAIN BELOW THE LEVEL OF INJURY OF THE SPINAL CORD

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IN THIS study information was obtained from 246 patients who had sustained injuries to the spinal cord and cauda equina. In addition, an intensive study was made on 50 patients, a few of whom were included in the first group.

The spontaneous pains of which these patients complain may be divided into three types. First may be mentioned pain referred to the segments about the lesion. Pain of this type may be a typical root pain, similar to that observed with any lesion affecting a root, such as tabes dorsalis or tumor; another form consists of pains in the same region, not of the characteristic quality of root pains but obviously originating from the nerve root. The second type is visceral or visceral referred pain, occurring in the course of dysfunction or disease or trauma of viscera and does not differ from that observed in normal man. The third type is pain which occurs distal to the level of the lesion. It is diffuse, often imperfectly localized and is described by such words as burning, tingling, stinging or pins and needles sensation. It partakes of the character of a paresthesia more than that of simple pain. Eighty per cent of the patients with this type of pain stated that it is most fittingly described as "burning."

In lesions of the cauda equina pain of the last type is difficult to differentiate from distal formication, such as may occur from a root lesion. The localization of this pain is often inconstant, even in individual patients, but is usually felt diffusely in the soles, in the lower extremities and in the abdominal wall. Relatively soon

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after injury the pain is sufficiently intense that the patient will spontaneously complain bitterly and ask for relief. Often addiction to narcotics has developed, and some surgical procedure, such as posterior root section or chordotomy, has been employed.

The spontaneous complaint of "burning" pain is made in most cases soon after injury. In a survey in 1947 such a complaint was made in 82 per cent of the cases. As time passed, the pain diminished, its threshold increased or it receded in consciousness and its presence was elicited only on direct questioning. In some cases even direct questioning failed to reveal its presence. It is now rare to find cases of the war material in which severe pain of this character is present, and there usually exists only a well repressed awareness of easily borne distress.

It should be pointed out that an increase in this type of pain which may occur in the event of intercurrent disease, surgical procedures, environmental changes, etc., should not be interpreted as evidence of integrity of the sensory pathway.

To explain the "spontaneous" diffuse burning and other types of pain which are felt distal to the level of injury to the spinal cord, many theories have been proposed. Some have evoked the participation of the sympathetic nervous system. We propose that the site of origin of this pain is the distal end of the segment proximal to the lesion of the spinal cord.

Frequently in some cases of injuries to the spinal cord a phantom sensation of recognition of existence of the lower extremities is present, and the patient seems to feel different positions of the extremities. When for some reason a lower extremity may have been amputated at the hip, this phantom sensation persists and is referred not only to the remaining, but to the amputated, extremity. When before amputation a distal burning pain had been present in both extremities, it was found to persist after amputation. It follows that in these cases the burning pain was not the result of sensory stimuli originating in the extremity or of efferent sympathetic impulses from the spinal cord, acting by chemical mediators on the sensory end organs of the extremity. In three such cases a transverse lesion of the spinal cord was found combined with phantom sensations of burning pain in the extremities, followed later by amputation with persistence of pain.

In a number of cases a spinal fluid block was present at the site of injury. When a spinal anesthesia was effected below the level of the lesion, suppressing all spasms and reflex activity, the distal burning pain did not disappear. Interruption of sensory impulses entering the spinal cord below the level of the lesion by any pathway did not abolish this pain.

In four cases of spinal fluid block spinal anesthesia was effected above the level of the lesion and confirmed by ascent of sensory loss. In these cases the distal pain gradually disappeared, remained absent and at a time compatible with the patient's recovery from anesthesia gradually and completely returned. A protocol of one of these cases may illustrate this observation.

In a case of physiologically complete lesion of the spinal cord at the eleventh thoracic segment, a fine plastic tubing was introduced into the spinal canal through a needle. The fact that the needle entered the spinal canal above the spinal fluid block had been demonstrated by normal manometric studies.

Crushing and burning pain had spontaneously been complained of in both lower extremities, and phantom sensation of the limbs had been present.

Three minutes after injection of 1 cc. of 0.5 tetracaine hydrochloride in 10 per cent dextrose solution, the patient experienced a feeling of warmth spreading over his extrem-

ities; eight minutes later, the phantom sensation of his limbs disappeared, and the burning and crushing pain had diminished; nine minutes later all pain had disappeared.

Eighteen minutes after this, awareness of the left lower extremity returned; 24 minutes later, awareness of the right lower extremity returned, and a detectable burning pain was again felt in the extremities. Fifty-six minutes later the crushing pain began to return, and thereafter both the burning and the crushing pain increased in intensity until three hours later, when they were of the same intensity as that experienced before the anesthesia.

It would appear to us that this distal burning pain originates from the distal end of the segment proximal to the injury of the spinal cord. This pain is quite similar to the pains referred from a neuroma at the end of the proximal segment of an injured peripheral nerve.

In the case of a severe injury to the spinal cord it has at times been proposed that suitable stimulation of structures innervated by segments distal to the point of injury can result in pain because the impulses, such as those from an extremity, are said to find their way into the proximal segment of the spinal cord by way of the sympathetic nerve fibers. The sensations evoked by stimuli were usually reported to have originated from subcutaneous structures, viscera and blood vessels, etc., although particular stimuli applied to the skin, such as faradism, have likewise been reported to produce pain. Generally such reports have been the result of experimental study on a few animals. We report on our observations only to record, perhaps unnecessarily, the absence of such pain in a significantly large material.

We have carefully studied a group of 50 patients with complete physiological interruption of the spinal cord to determine whether stimuli which in the intact person would produce pain could be perceived by these patients. In every one of these patients some disease or injury which should result in pain had occurred one or more times.

With respect to the skeletal nervous system, the following injuries, diseases or operative procedures without anesthesia produced no pain: fractures, 10 cases; dislocations, 5 cases; burns, lacerations or abrasions, 37 cases; decubitus ulcers, 235 cases; extensive surgical repairs of decubitus ulcers with plastic skin flaps without anesthesia, 98 cases; innumerable dressings of such decubitus ulcers; suprapubic cystotomies, 9 cases; orchidectomy, 4 cases; nephrolithectomy, 1 case, and numerous spinal punctures.

With respect to the visceral system, no pain was experienced by eight patients with 14 attacks of orchitis, the level of the lesion ranging from the sixth cervical to the twelfth thoracic segment; by eight patients with 11 attacks of epidydimitis, the level of the lesion ranging from the eighth cervical to the second thoracic segment; by 12 patients with 27 attacks of cystitis, the lesions ranging from the sixth cervical to the first lumbar segment; by three patients with four attacks of kidney stone, the level of the lesion ranging from the sixth cervical to the twelfth thoracic segment, and by five patients with eight episodes of spontaneous passage of bladder stone, the lesions ranging from the second to the ninth thoracic segment. No pain was experienced by five patients during orchidectomy, the lesions ranging from the second to the tenth thoracic segment; by two patients during ureteral catheterization, with lesions at the eighth cervical and ninth thoracic segments, respectively; by three patients during resection of the neck of the bladder, the level of the lesion ranging from the seventh cervical to the ninth thoracic segment; by 17 patients

during suprapubic cystotomies, the lesion ranging from the sixth cervical to the tenth thoracic segment; by 10 patients with nine litholapaxies, the lesions ranging from the fifth cervical to the tenth thoracic segment, and by 12 patients with 27 cystoscopies, the lesions ranging from the sixth cervical to the first lumbar segment, as well as in innumerable passages of urethral catheters.

Four patients experienced pain, one with a lesion at the tenth thoracic segment, when a kidney stone was removed; another with a lesion at the twelfth thoracic segment, when a kidney stone was removed; another with a lesion at the tenth thoracic segment, during an attack of orchitis, and one with a lesion at the first lumbar segment, during cystoscopy and attacks of cystitis. In all these patients it appeared to us that the sensory fibers responsible for pain entered the spinal cord above the level of the lesion. Exception to this rule might be taken in the case of pain from orchitis with a lesion at the tenth thoracic segment.

From this study we shouuld conclude that, both for the skeletal and for the visceral systems, stimuli designed to produce pain, even those of great intensity from blood vessels, bones, other subcutaneous tissues and viscera, send impulses over the ordinary sensory pathways in the spinal cord.

CONCLUSIONS

The site of origin of distal "burning" pain associated with severe injuries of the spinal cord is the distal end of the segment proximal to the level of the lesion.

In cases of severe injury to the spinal cord, no pain is felt when the structures below the level of injury are subjected to disease or to gross trauma.

PROGNOSIS IN TOPECTOMIES AND LOBOTOMIES RELATIVE TO BODY TYPE

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IN 1947 a series of operations designated as "topectomies" were performed on a group of chronic schizophrenic patients at the New Jersey State Hospital, at Greystone Park. Since the studies of these patients were undertaken by both the hospital staff and members of Columbia University College of Physicians and Surgeons, the work became known as the Columbia-Greystone I Project. The numerical designation was necessary, since two subsequent investigations were carried out by essentially the same group of associates.

The topectomies consisted of selective partial ablations of the frontal lobe and have been reported in full detail.[1] Various Brodmann areas were removed, and there was a strong impression that extirpation of Brodmann areas 8, 9, 10 and/or 46 were distinctly beneficial, in contrast to removal of certain other areas (6, 11, 24, 44, 45 and 47).

A portion of the patients did not have topectomies but served as controls. Subsequently, a number of these controls, as well as some of the topectomized patients who failed to improve, were lobotomized.

An elaborate and exhaustive series of tests and measurements were performed both before and after operation. These are also reported in detail elsewhere. There were, however, two studies not previously reported: the sexual histories of the patients, data on which were collected by Dr. Alfred Kinsey, and the somatotype studies, done under the direction of Dr. William H. Sheldon.[2] It is to be hoped that these will ultimately be published.

We have recently reported on finding statistically valid relations between prognosis and somatotype in a series of some 450 consecutive schizophrenic patients admitted to a Veterans Hospital,[3] so that a natural curiosity existed as to the relation of prognosis to body type in the patients of the Columbia-Greystone I Project.

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2. Sheldon, W. H.: Varieties of Human Physique, New York, Harper & Brothers, 1940; Varieties of Temperament, New York, Harper & Brothers, 1942; Varieties of Delinquent Youth: An Introduction to Constitutional Psychiatry, New York, Harper & Brothers, 1949.

3. Kline, N. S., and Tenney, A. M.: Constitutional Factors in the Prognosis of Schizophrenia, Am. J. Psychiat. **107**:434, 1950.

Since one of us (N. S. K.) was one of the Columbia-Greystone associates and was also working in the field of somatotyping, both sets of data were available, and permission was obtained for their release.

The somatotype studies on the female patients were incomplete and the total number was small, but data on 29 of the 30 male patients were complete. This report deals only with these male schizophrenics.

TABLE 1.—*Disposition of Patients After Three Years in Relation to Somatotypes*

Dominant Somatotype	Total No. of Patients	No. of Patients			
		Still Hospitalized	Discharged	Paroled or on Trial Visit	Dead
Endomorphy	2	1	1	0	0
Mesomorphy and endomorphy equal	3	2	0	1	0
Mesomorphy	10	3	6	1*	0
Mesomorphy and ectomorphy equal	1	0	0	1	0
Ectomorphy	10	7†	1	0	2
Ectomorphy and endomorphy equal	1	0	0	1	0
Endomorphy, mesomorphy and ectomorphy equal	2	2	0	0	0
Total	29	15	8	4	2

* Patient subsequently returned to hospital.
† Number includes one patient who escaped.

TABLE 2.—*Percentage Distribution of Mesomorphs as Compared with Other Somatotypes Relative to Discharge*

	Dominantly Mesomorphic, %	Other Somatotypes, %
Discharged	60	10.5
Still on active hospital rolls, dead or escaped	40	89.5

TABLE 3.—*Percentage Distribution of Discharges Relative to Somatotype and Operative Procedure*

Discharged	Areas 8, 9, 10 and/or 46	Other Areas	Lobotomies	Controls Not Operated on
Mesomorphs	100%	*	50%	40%
Other somatotypes	20%	0%	0%	16.6%

* No cases.

Exact somatotype ratings are available, but for the present communication it is simpler and equally valid to consider the body type in terms of the dominant components. This method provides nine possible categories of body type. The categories and the number of patients falling into each are presented in table 1. (The endomorphs are disposed toward adiposity; the mesomorphs, toward muscularity, and the ectomorphs, toward linearity and fragility.[4]

If comparisons are made between the dominantly mesomorphic type and other body types, as would be indicated by our previous study, a better prognosis for the mesomorphs is clearly preponderant.

4. For more complete description of somatotypes, see Sheldon.[2]

The evidence favors the conclusion that mesomorphy is related to prognosis, since the differences noted in table 2 are at better than the 2 per cent confidence level (chi-square of 5.6).

The better prognosis for the mesomorphs was not due to fortuitous inclusion in one particular operative group. Table 3 demonstrates that mesomorphs had more favorable results, regardless of operative procedure (or lack of it).

COMMENT

If the patient subjected to either a topectomy or a lobotomy is not a mesomorph, the prognosis for a favorable outcome is less than 1 in 10. Of the 13 nonmesomorphs operated on in our series, only one was discharged. On the other hand, four of the five mesomorphs in our series who had either lobotomy or topectomy have been discharged, and the remaining patient (with lobotomy) was on trial visit but has been at least temporarily returned to the hospital. The use of psychosurgical procedures on nonmesomorphs should be undertaken with caution.

STUDIES ON THE IRON CONTENT OF CEREBROSPINAL FLUID IN DIFFERENT PSYCHOTIC CONDITIONS

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THE METABOLISM of iron and the iron content of the various organs concerned with the formation and destruction of erythrocytes and hemoglobin have been thoroughly investigated in recent years, both in experimental animals and in man.[1] The presence and importance of iron as a regular constituent of the cytochrome-oxidase system involved in the respiratory processes of the cell are now well recognized.[2] It is therefore not surprising that the iron content of the brain, which has a high oxygen consumption, has become a matter of interest to neuropathologists, biochemists and psychiatrists.

Biondi [3] and Guizzetti [4] were the first to draw attention to the fact that certain gray masses in the adult brain of man and domestic animals contain a considerable amount of iron, which can be clearly demonstrated in macroscopic brain sections with potassium ferrocyanide or ammonium sulfide. This reaction is absent in the brain of the fetus and the newborn. Müller [5] confirmed and extended Guizzetti's findings and demonstrated the iron reaction also in microscopic sections.

A systematic anatomic study of the iron content of the brain was conducted by Spatz.[6] This author confirmed the findings of the previous investigators and showed that the gray masses of the brain can be divided into four groups according to the intensity of the macroscopic iron reaction, as obtained with prussian (aniline) blue and ammonium sulfide. The first group, in which the iron reaction appears first and is most pronounced, comprises the globus pallidus and the substantia nigra. The second group consists of the red and the dentate nuclei, the striate

From the Verdun Protestant Hospital.
Miss Dorothy K. Turnbull, B.Sc., of the department of biochemistry of McGill University, performed the chemical analyses.

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6. Spatz, H.: Über den Eisennachweis im Gehirn, besonders in den Zentren des extrapyramidalmotorischen Systems, Ztschr. f. d. ges. Neurol. u. Psychiat. **77**:261-390, 1922.

body (caudate nucleus and putamen) and the subthalamic body of Luys. In this group the iron reaction appears later and is somewhat weaker. In the third group, comprising the mamillary bodies, parts of the thalamus, the cerebral and cerebellar cortex and the central gray matter around the third ventricle, the iron reaction appears after a considerable delay and is usually weak. The fourth group, consisting of the spinal gray matter, the spinal and sympathetic ganglia and the inferior olivary nucleus, does not show any iron reaction. Spatz also observed that the fetal brain never shows a positive iron reaction, whereas the iron content of the fetal liver and spleen is found to be very high.

Spatz, furthermore, investigated the microscopic iron reaction of pathological brains. He found iron to be consistently increased in the cortex of patients with dementia paralytica in areas around cerebral hemorrhages. He also observed a particularly strong reaction in the centers of his first and second group in cases of extrapyramidal diseases of the akinetic type. Spatz [7] stated the opinion that the iron content of the brain should be considered an indicator of another factor connected with oxygen metabolism. The iron of the brain seems to be independent of the iron content of the liver and spleen and is apparently not related to increased destruction of erythrocytes, as, for instance, in pernicious anemia.

Tretiakoff and Caesar,[8] Verciani [9] and Marinesco and Draganesco [10] confirmed the observations of the previous investigators. The last-mentioned authors elaborated on the fact that in various pathological processes and in the senium the iron content of the extrapyramidal centers is likely to increase and to be modified. This view was shared by Strassmann,[11] who stated that the iron content of the brain increases proportionally with age.

Aside from these anatomic investigations, several determinations of the amount of iron in the brain have been made by quantitative chemical analysis.

Tingey,[12] in examining normal brains, found the highest iron content in the globus pallidus and in the substantia nigra. The cerebral and cerebellar cortex and the white matter showed a lower iron content. These findings, which were made similarly with fresh and with dried material, show therefore a striking parallelism to the anatomic observations and were later confirmed by Cumings.[13] Tingey, furthermore, showed that the cortex in cases of dementia paralytica contains more iron than the normal cerebral cortex.

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7. Spatz, H.: Über Stoffwechseleigentümlichkeiten in den Stammgangiien, Ztschr. f. d. ges. Neurol. u. Psychiat. **78**:641-648, 1922.

8. Tretiakoff, C., and Caesar, O.: Étude histochimique des composés du fer dans l'écorce cérébrale et cérébelleuse des aliénés, Rev. neurol. **2**:220-242, 1926.

9. Verciani, A.: Il ferro nel sistema nervoso centrale in condizioni normali e patologiche, Rassegna di studi psichiat. **14**:141-168, 1925.

10. Marinesco, G., and Draganesco, S.: Recherches sur le métabolisme du fer dans les centres nerveux, Rev. neurol. **2**:385-398, 1923.

11. Strassmann, G.: Hemosiderin and Tissue Iron in the Brain, Its Relationship, Occurrence and Importance: Study on 93 Human Brains, J. Neuropath. & Exper. Neurol. **4**:393-401, 1945.

12. Tingey, A. H.: The Iron, Copper and Manganese Content of the Human Brain, I., J. Ment. Sc. **83**:452-460, 1937; The Iron Content of the Human Brain, II., ibid. **84**:980-984, 1938.

13. Cumings, J. N.: The Copper and Iron Content of Brain and Liver in the Normal and in Hepatolenticular Degeneration, Brain **71**:410-415, 1948.

Freeman,[14] in extensive investigations on the iron content of the cerebral cortex in various mental disorders with histochemical and quantitative chemical methods, found the amount of iron in the brain considerably lower in his schizoid group than in his other groups. The iron of the brain, in his opinion, plays an important role in the oxidation-reduction system of the nerve cells. He advanced the theory that the psychotic process in schizophrenia is associated with impaired utilization of oxygen by the brain cells, which are handicapped by their lower iron content.

The iron in the cerebrospinal fluid has recently been investigated by a number of workers. Beck [15] found very low iron values for the spinal fluid of schizophrenic patients. Buscaino [16] found 34 micrograms per 100 cc. for normal persons and almost normal iron values for 30 schizophrenic patients when the mean of the group was taken. However, a moderate, but consistent, increase in the iron of the spinal fluid appeared in catatonic patients, particularly in the early months of the illness. Tramontana,[17] who performed parallel determinations of iron in the serum and in the spinal fluid in 20 normal persons, gives the range of the spinal fluid iron as 23 to 52 micrograms and the mean as 35 micrograms, per 100 cc. In his matched series, there was no difference with respect to the spinal fluid iron between men and women, and no precise relation to the serum iron could be demonstrated. The ratio of serum iron to spinal fluid iron approximated 3:1. The same author reported on his findings in cases of untreated tuberculous meningitis. He showed that the serum iron was moderately reduced (50 to 70 micrograms per 100 cc.), whereas the spinal fluid iron was reduced to very low values (8 to 10 micrograms per 100 cc.), with a considerable increase in the ratio of the serum iron to spinal fluid iron. For that reason, Tramontana stated the belief that the iron content of the spinal fluid does not depend on simple physiochemical mechanisms, but, rather, is regulated by biologic factors of a more complex nature.

It is the purpose of this paper to report on the iron content of the spinal fluid in a number of patients with various psychiatric conditions.

MATERIAL

The iron content was determined in 103 individual samples of spinal fluid obtained from 98 patients. Table 1 gives the essential data on each patient. In 5 cases the determination was repeated after a therapeutic procedure had been carried out, i. e., electric convulsion or malaria therapy. Patients were chosen according to certain diagnostic and clinical criteria, which served to designate the following five groups:

Group	No. of Patients
Nonpsychotic disorders	18
Organic psychoses	34
Schizophrenia, nondeteriorated	20
Schizophrenia, deteriorated	13
Miscellaneous psychoses	13

This division was established before individual patients were selected, and each patient was placed in his group before his spinal fluid iron was known.

14. Freeman, W.: Deficiency of Catalytic Iron in the Brain in Schizophrenia, Arch. Neurol. & Psychiat. **24**:300-310 (Aug.) 1930.

15. Beck, G.: Über den Eisengehalt im Liquor, Inaug. Dissert., Jena, 1939.

16. Buscaino, G. A.: Il ferro labile nel liquido cefalo rachidiano, Acta neurol. **1**:3, 1946; Il ferro labile nel liquor di schizofrenici, ibid. **1**:113, 1946.

17. Tramontana, C.: Sulla presenza e sul significato del ferro nel liquido cefalorachidiano, Boll. soc. ital. biol. sper. **24**:615, 1948.

The first group (nonpsychotic) was made up of patients who had been committed because of conduct disorders or social difficulties but who had at no time shown manifestations of a psychotic process. This group, of 18 patients, comprised 9 patients with simple mental deficiency, 4 with psychopathic personality, 3 with alcoholic addiction and 2 with hysteria.

The second group (organic psychosis) consisted of patients with a variety of conditions, all of which were characterized by psychosis associated with "organic" or structural cerebral disease. The following diagnostic entities were contained in this group: dementia paralytica, 19 patients; psychosis with parkinsonism, 6 patients; psychosis with cerebral arteriosclerosis, 3 patients; senile dementia, 2 patients; psychosis with chorea, 2 patients; Alzheimer's disease, 1 patient; Korsakoff's psychosis, 1 patient.

The third and fourth groups were composed of 20 nondeteriorated and 13 deteriorated schizophrenic patients, respectively. Our criteria of deterioration consisted in (*a*) chronicity of the schizophrenic psychosis; (*b*) complete, or almost complete, loss of contact with reality; (*c*) pronounced loss of drive, and (*d*) inappropriate affect. All these criteria had to be met by patients who were placed in the fourth group, that of deteriorated schizophrenics. All the patients in this group would clinically be classified as hebephrenic or catatonic, i. e., as having the "nuclear" type of schizophrenia. In the third group, that of nondeteriorated schizophrenic patients, one also finds catatonic and hebephrenic patients, but in the acute stages, as well as a number with the chronic paranoid form.

We felt that the traditional types of schizophrenia were unsatisfactory divisions for our purpose of establishing groups for statistical comparison, since it is often difficult or impossible to obtain an agreement on the diagnostic classification of a patient during an acute schizophrenic breakdown. Chronicity of the schizophrenic psychosis has been shown by some investigators[18] to produce physiological changes. We have thought it justified, however, to select personality deterioration, in addition to the mere passage of time, as the criterion for the division of our schizophrenic groups, since the damage produced in a deteriorated hebephrenic patient after five years is certainly more substantial than that present in a patient with paranoid schizophrenia of 10 years' standing with a well preserved personality.

The fifth (miscellaneous) group represents a number of psychotic patients with different diagnoses. The group, of 15 patients, comprised 3 with manic-depressive psychosis, 2 in the manic phase and 1 in the depressed phase; 4 with involutional melancholia; 2 with reactive depressions; 1 with a paranoid condition and 2 with mongolism. The cases in this group were not collected systematically, but the patients were examined as they presented themselves in order to obtain further background material and with a view to obtaining possible leads in the systematic investigation of other diagnostic groups. We were also interested in the effects of electric convulsion therapy on spinal fluid iron, and some patients in this group were receiving this type of treatment. All the first iron determinations were made on patients who had not received electric convulsion or insulin shock therapy within six months prior to the lumbar puncture.

We have no "controls" in our material, but it can be assumed that in an unselected group of normal control subjcts a certain number of alcoholic, mentally defective, neurotic and psychopathic persons might be found, so that the difference between such a control group and our nonpsychotic group would appear to be one of degree rather than of quality.

METHOD

The total iron content was determined in the following manner:

A suitable aliquot (2.0 to 4.0 ml.) of the cerebrospinal fluid was pipetted into a 50 ml. beaker; 5 ml. of concentrated nitric acid (reagent grade) was added, and the solution was evaporated to dryness on a steam bath. The white residue was dissolved in 8.0 ml. of sodium acetate buffer, p_H 4.5, and 2.0 ml. of stock solution of o-phenanthroline was added to develop the color. The o-phenanthroline stock solution contained 50 ml. of saturated sodium acetate

18. (*a*) Pfister, H.: Disturbances of the Autonomic Nervous System in Schizophrenia and Their Relations to the Insulin, Cardiazol and Sleep Treatments, Am. J. Psychiat. (supp.) **94**:109-118, 1938. (*b*) Ferroni, A., and Lipani, G.: Curve sideremiche da carico in amenti e schizofrenici, Acta neurol. **3**:568-583, 1948.

solution (about 12.5 Gm. per 100 ml. of water), 50 ml. of o-phenanthroline solution in water and 0.25 Gm. of hydrazine sulfate. The beaker was covered with aluminum foil to prevent evaporation and allowed to stand overnight to insure complete development of the color. The sample then was transferred to the colorimeter tube, and the color density was read in an Evelyn colorimeter, using filter 490, after a zero setting had been established with a blank containing only the reagents but otherwise subjected to the same treatment as was the unknown. The iron concentration in the sample was obtained by reference to a standard curve and was finally expressed as milligrams of iron per 100 ml. of spinal fluid.

In such a determination iron contamination of glassware and reagents must be avoided. It is important that iron-free nitric acid be used for digestion of the samples.

In this study a standard curve was prepared with each set of determinations, since sodium acetate, even in reagent grade, contains some iron. It is well to repeat the preparation of the standard curve also with each new batch of buffer or other reagent. The practice of the frequent repetition of determination of the standard curves eliminated the danger of error from high iron values due to iron-contaminated reagents. Recoveries of added ionized iron by this method were in the range of 98 to 102 per cent.

Careful consideration was given to the comparison of the iron content and the spinal fluid findings as determined with the routine laboratory methods: the Pandy reaction, the cell count, the Wassermann reaction and the colloidal gold curve. It was found that the iron content was independent of the other findings in our material. Special attention was paid to the possibility that the iron content might have been influenced by an occasional erythrocyte contained in the spinal fluid, although all hemorrhagic fluids were excluded. Nevertheless, in counting the leukocytes, the finding of an occasional erythrocyte was noted separately. No influence of these rare erythrocytes on the iron content of the spinal fluid could be detected. In some of these fluids the iron content was low; in others it was found around the mean. It should be noted, however, that the fluids with an exceedingly high iron content were found free of even single erythrocytes.

RESULTS

The results of our investigations are given in tables 1 and 2.

TABLE 1.—*Individual Data on Case Material*

Number	Age	Sex	Diagnosis	Iron (Mg./100 Ml.) in Cerebrospinal Fluid
1	23	F	Mental deficiency	0.033
2	39	M	Mental deficiency	0.037
3	66	M	Cerebral arteriosclerosis	0.050
4	34	F	Paranoid condition	0.060
5	15	F	Psychopathic personality	0.050
6	26	F	Hysteria	0.050
7	38	F	Mental deficiency	0.035
8	44	M	Mental deficiency	0.032
9	49	F	Chronic chorea	0.042
10	34	M	Mental deficiency	0.050
11	42	F	Mental deficiency	0.038
12	32	M	Mental deficiency	0.040
13	73	M	Parkinsonism	0.074
14	39	M	Parkinsonism	0.083
15	23	M	Mental deficiency	0.028
16	43	M	Mental deficiency	0.030
17	19	F	Schizophrenia, catatonic	0.054
18	29	F	Korsakoff's psychosis	0.017
19	36	M	Parkinsonism	0.040
20	57	M	Dementia paralytica	0.026
21	52	M	Dementia paralytica	0.030
22	61	M	Dementia paralytica	0.036
23	55	F	Schizophrenia, paranoid	0.024
24	30	M	Dementia paralytica	0.048
25	51	M	Dementia paralytica	0.038
26	39	M	Parkinsonism	0.056
27	62	M	Parkinsonism	0.068
28	73	M	Parkinsonism	0.048

TABLE 1.—*Individual Data on Case Material—Continued*

Number	Age	Sex	Diagnosis	Iron (Mg./100 Ml.) in Cerebrospinal Fluid
29	62	M	Dementia paralytica	0.120
30	53	M	Dementia paralytica	0.067
31	40	M	Dementia paralytica	0.046
32	51	M	Dementia paralytica	0.060
33	45	M	Dementia paralytica	0.020
34	58	M	Dementia paralytica	0.032
35	52	F	Dementia paralytica	0.068
36	45	F	Dementia paralytica	0.048
37	34	F	Schizophrenia, paranoid	0.028
38	45	F	Dementia paralytica	0.022
39	61	F	Alcoholism	0.005
40	46	F	Alcoholism	0.032
41	26	F	Psychopathic personality	0.013
42	71	M	Manic-depressive psychosis, depressed	0.011
43	18	M	Mongolism	0.083
44	84	M	Senile psychosis	0.043
45	29	M	Schizophrenia, paranoid	0.025
46	22	M	Schizophrenia, paranoid	0.022
47	60	M	Schizophrenia, paranoid	0.035
48	75	F	Senile chorea	0.070
49	20	M	Mongolism	0.028
50	58	M	Dementia paralytica	0.053
51	49	M	Dementia paralytica	0.020
52	73	M	Alcoholism	0.038
53	54	M	Alzheimer's disease	0.020
54	36	M	Schizophrenia, catatonic, deteriorated	0.053
55	35	M	Schizophrenia, catatonic, deteriorated	0.043
56	26	M	Schizophrenia, hebephrenic, deteriorated	0.050
57	52	M	Schizophrenia, catatonic, deteriorated	0.027
58	67	M	Dementia paralytica	0.047
59	37	M	Schizophrenia, paranoid	0.047
60	28	M	Schizophrenia, mixed type	0.182
61	31	M	Schizophrenia, paranoid	0.050
62	62	M	Psychopathic personality	0.055
63	25	M	Schizophrenia, paranoid	0.052
64	33	F	Schizophrenia, mixed type	0.033
65	53	F	Cerebral arteriosclerosis	0.028
66	48	M	Involutional depression	0.043
66A	Repetition six weeks later			0.022
67	62	M	Reactive depression	0.053
68	69	M	Cerebral arteriosclerosis	0.070
69	60	M	Dementia paralytica	0.035
69A	Repetition six weeks later			0.020
70	62	F	Manic-depressive, psychosis, depressed	0.040
70A	Repetition six weeks later			0.030
71	39	M	Reactive depression	0.060
71A	Repetition six weeks later			0.073
72	38	M	Schizophrenia, hebephrenic, deteriorated	0.075
73	45	M	Involutional depression	0.048
74	38	F	Schizophrenia, hebephrenic, deteriorated	0.117
75	24	F	Schizophrenia, hebephrenic, deteriorated	0.065
76	22	F	Psychopathic personality	0.093
77	41	M	Dementia paralytica	0.028
78	39	F	Schizophrenia, catatonic, deteriorated	0.360
79	32	F	Schizophrenia, catatonic, deteriorated	0.057
80	39	F	Schizophrenia, hebephrenic, deteriorated	0.040
81	43	F	Schizophrenia, catatonic, deteriorated	0.017
82	46	F	Involutional depression	0.075
83	39	F	Schizophrenia, catatonic	0.025
84	33	F	Schizophrenia, simple, deteriorated	0.043
85	39	F	Schizophrenia, catatonic, deteriorated	0.027
86	29	M	Schizophrenia, catatonic	0.035
86A	Repetition 4 weeks later			0.052
87	45	M	Involutional depression	0.030
88	17	M	Schizophrenia, hebephrenic	0.013
89	30	M	Schizophrenia, paranoid	0.023
90	19	M	Schizophrenia, catatonic	0.025
91	31	F	Schizophrenia, paranoid	0.027
92	23	F	Hysteria	0.023
93	29	F	Schizophrenia, catatonic	0.028
94	55	M	Manic-depressive psychosis, manic type	0.022
95	42	F	Manic-depressive psychosis, manic type	0.030
96	71	M	Senile psychosis	0.050
97	42	M	Schizophrenia, catatonic	0.028
98	41	M	Schizophrenia, paranoid	0.037

The range of iron was found to lie between 0.005 and 0.360 mg. per 100 ml. The mean was 0.048 mg. per 100 ml., and the standard deviation, 0.040. A closer inspection of table 1 reveals, however, that four spinal fluids obtained from four patients (29, 60, 74 and 78) had an iron content higher than 0.100 mg. per 100 ml. For statistical reasons, we omitted these cases from the following evaluation, since they were too far removed from the mean, exceeding almost the mean plus twice the standard deviation. When these four values were eliminated from a series of 103 samples, the standard deviation was reduced to less than half its former value. It is to be noted, however, that their inclusion in the statistical tabulation would actually have emphasized our results.

When these four cases are eliminated, we obtain the following general results, as shown in line 7 of table 2. For 99 spinal fluids obtained from 94 patients, the range of iron content was found to lie between 0.005 and 0.093 mg. per 100 ml.; the mean was 0.042 mg. per 100 ml., and the standard deviation, 0.019.

In our nonpsychotic group, which in some way approached a control group, the range of iron content was between 0.005 and 0.093 mg. per 100 ml., the mean

TABLE 2.—*Diagnostic Classification and Statistical Data*

Group	Number of Cases	Number of Spinal Fluids	Average Age	Iron, in Mg./100 Cc.		Standard Deviation
				Range	Mean	
Nonpsychotic	18	18	37	0.005-0.093	0.038	0.019
Organic	33	34	54	0.017-0.090	0.047	0.019
Schizophrenic, nondeteriorated	19	20	33	0.013-0.054	0.032	0.011
Schizophrenic, deteriorated	11	11	35	0.017-0.075	0.045	0.018
Schizophrenic (whole group)	30	31	34	0.013-0.075	0.037	0.015
Miscellaneous	13	16	45	0.011-0.080	0.047	0.024
Total after omission of cases 29, 60, 74, 78	94	99	43	0.005-0.093	0.042	0.019
Total	98	103	43	0.005-0.360	0.048	0.040

0.038 mg. per 100 ml. and the standard deviation 0.019. Our values approach closely those of Buscaino and Tramontana, who found 0.034 and 0.035 mg. per 100 cc., respectively, for normal controls. Vonkennel and Tilling, as quoted by Tramontana, reported 0.032 mg. per 100 cc. in their series. We were interested to see whether the age of the patient had any influence on the iron content of the spinal fluid. The average age in this group was 37 years. The patients were divided into two groups, one comprising 9 patients between 15 and 35 years, and the other, 9 patients of more than 35 years. The iron values for these two groups showed no significant difference.

In our group with psychoses of organic origin the average age was 54 years. The iron content of the spinal fluid was scattered between 0.017 and 0.090 mg. per 100 ml.; the mean was 0.047 mg. per 100 ml., and the standard deviation, 0.019. This mean was higher than that for our nonpsychotic group, but the difference between the two means was found not to be statistically significant.

Within the group with organic psychoses two special subgroups seemed of interest, the patients with dementia paralytica and the patients with paralysis agitans, in view of the fact that histochemical examinations have been reported to show a higher iron content in the brain in these conditions. Nineteen spinal fluids of 18 patients with dementia paralytica showed an iron content in the range

of 0.020 to 0.090 mg. per 100 ml.; the mean was 0.044 mg. per 100 ml., and the standard deviation, 0.019. Although higher than the value for the nonpsychotic group, the difference of the means was statistically not significant. The small group of patients with paralysis agitans, on the other hand, comprising six spinal fluids from six patients, with an average age of 54 years, had an iron content ranging from 0.040 to 0.083 mg. per 100 ml. The mean was 0.058 mg. per 100 ml., and the standard deviation, 0.016. The difference between the means of this subgroup with organic psychoses and the nonpsychotic group was found to be statistically significant. These results are in accordance with the findings of Ferroni and Indovina,[19] who reported a high iron content of the spinal fluid with reduced serum iron in cases of postencephalitic parkinsonism.

The schizophrenic group as a whole comprised 30 patients with 31 spinal fluids; 3 patients and three spinal fluids were excluded, for the reasons mentioned above. The average age for our entire schizophrenic group was 34 years; the iron content of the spinal fluid varied between 0.013 and 0.075 mg. per 100 ml., with a mean of 0.037 mg. per 100 ml. and a standard deviation of 0.015. Compared with that for the nonpsychotic group, the difference of the means was not significant, but there was a statistically significant difference between the means for the schizophrenic group as a whole and that for the "organic" group as a whole.

When the schizophrenic group was divided into nondeteriorated and deteriorated patients, the nondeteriorated schizophrenic patients were found to have a range of 0.013 to 0.054 mg. per 100 ml., a mean of 0.032 mg. per 100 ml. and a standard deviation of 0.011. The corresponding values for the deteriorated group were a range of 0.017 to 0.075 mg. per 100 ml., a mean of 0.045 mg. per 100 ml. and a standard deviation of 0.018. The difference between the means for the two groups was found to be statistically significant. It was found, furthermore, that the difference of the means for the nondeteriorated schizophrenic subjects and the means for the "organic" group was highly significant, whereas no significant difference could be found between the values for the "organic" group and the deteriorated schizophrenic patients. In other words, statistically the deteriorated group was very similar to the group with organic psychoses, whereas the nondeteriorated schizophrenic patients behaved like our patients with nonorganic psychoses so far as the spinal fluid is concerned.

The average age for our miscellaneous group was 45 years. The range of iron content was 0.011 to 0.090 mg. per 100 ml.; the mean, 0.047 mg. per 100 ml., and the standard deviation, 0.024. No conclusions can be drawn from the results obtained in this group because of its heterogeneous composition, which is also expressed in its comparatively high standard deviation.

COMMENT

The mechanism of production of cerebrospinal fluid is not yet clearly understood. Several workers have shown, however, that the spinal fluid is not simply a product of dialysis or ultrafiltration, but involves biologic activity of the par-

19. Ferroni, A., and Indovina, L.: Ferro labile nel siero e nel liquor nel parkinsonismo, Boll. soc. med.-chir. Catania **13**:271, 1945.

ticipating structures.[20] This has been demonstrated to hold true for organic, as well as for inorganic, constituents of the spinal fluid. The Donnan equilibrium, for example, does not govern its content of magnesium and phosphorus.[21] However, it seems a safe assumption that two sources of the spinal fluid iron have to be considered, that is, the blood and the brain. There is as yet no information available on the relative significance of the two sources. A high iron content of the spinal fluid may reflect an increase of the serum iron, an increased permeability of the hematoencephalic barrier or a process of elimination of iron from iron stores in certain parts of the brain. That, in turn, may be due either to an increased storage of iron or to a functional inability of the cells to hold a normal amount of iron.

Parallel investigations of serum iron and spinal fluid iron in normal, as well as in various pathological, conditions [22] have demonstrated that the spinal fluid content is relatively independent of fluctuations in the serum iron content. In certain conditions the two iron values have been observed to vary in opposite directions. Furthermore, variations in the serum iron, particularly an increase in the iron, are small in comparison with the range of variation found in the spinal fluid iron. One is inclined, therefore, to conclude that the brain cells are mainly responsible for the iron content of the spinal fluid.

A diminished iron content of the spinal fluid has been reported by several authors in acute inflammatory diseases of the central nervous system.[23]

At this point a brief review may be in place. It is now recognized that very little iron is lost from the organism except through hemorrhage. While the serum iron is reduced in inflammatory diseases, the tissue iron is increased at the site of the inflammatory process. Some authors believe that the reticuloendothelial system requires greater quantities of iron to serve as a catalyst in the increased cell metabolism which constitutes a defense reaction of the organism. It is, of course, possible that the parenchymatous cells also take an active part in such a reaction. These increased cellular requirements are met by an increased supply of available iron from the body fluids.

Methods which are available for the direct examination of cerebral metabolism through the determination of oxygen and glucose differences between blood samples taken from an artery and those from the internal jugular vein have shown reduced oxidative processes in certain organic diseases of the brain, while no definite change in either direction could be demonstrated in schizophrenic subjects.[24] However, a

20. Katzenelbogen, S.: The Cerebrospinal Fluid and Its Relation to the Blood: A Physiological and Clinical Study, Baltimore, Johns Hopkins Press, 1935.

21. Kral, A.; Stary, Z., and Winternitz, R.: Zur Frage der Liquorgenese, Ztschr. f. d. ges. Neurol. u. Psychiat. **122**:308-316, 1929.

22. Tramontana.[17] Ferroni and Lipani.[18b] Ferroni and Indovina.[19]

23. Buscaino.[16] Tramontana.[17]

24. Cameron, D. E.; Himwich, H. E.; Rosen, S. R., and Fazekas, J. F.: Oxygen Consumption in the Psychoses of the Senium, Am. J. Psychiat. **97**:566-572, 1940. Wortis, J.; Bowman, K. M., and Goldfarb, W.: Human Brain Metabolism: Normal Values and Values in Certain Clinical States, ibid. **97**:552-565, 1940. Himwich, H. E., and Fazekas, J. F.: The Oxygen Content of Cerebral Blood in Patients with Acute Symptomatic Psychoses and Acute Destructive Brain Lesions, ibid. **100**:648-651, 1944.

wide range of values has been reported for schizophrenic patients, indicating that schizophrenia may be associated with increased, as well as with reduced, cerebral metabolism.[25]

In consideration of the foregoing discussion, the following explanations for the variation in the iron content of different spinal fluids offer themselves:

In those diseases of the central nervous system which, as a rule, are not associated with increased iron content of the brain cells, an abnormally high amount of iron in the spinal fluid must be viewed as reflecting a reduced utilization of iron for the cellular metabolism, and thus it may be considered an indicator of decreased cellular activity. A decrease of iron in the spinal fluid in those conditions, on the other hand, may point to an increased want of iron in the brain cells and thus indicate heightened cellular activity, most likely as an expression of a defensive reaction.

In those diseases of the central nervous system in which a pathological increase of iron has been demonstrated in the brain tissue, an abnormally high iron content of the spinal fluid may be due either to a decrease of the cellular metabolism or merely to an overflow from the large iron deposits in the brain tissue. A decreased iron content of the spinal fluid in these cases, however, seems to present good evidence for greater utilization of iron in the cells which may require it for their increased metabolic activity.

Therefore, high spinal fluid iron in our cases of dementia paralytica or paralysis agitans may reflect lowered cellular activity or merely an overflow of the increased storage iron. In both conditions abnormally high amounts of iron have been demonstrated by histochemical, as well as quantitative, methods in the cortex and the extrapyramidal system, respectively. A low iron content of the spinal fluid of patients with these diseases, on the other hand, must be interpreted as a strong indication of heightened cellular activity. While a number of our patients with dementia paralytica gave comparatively low iron values, all of our patients with paralysis agitans had spinal fluid iron values above average.

In our group of schizophrenic patients the clinical division between acute and deteriorated patients parallels closely the quantitative differences of the spinal fluid iron. In the acute cases it is low, in fact lower than in the nonpsychotic group, and one might well consider this an expression of greater cellular activity in the acute phase of schizophrenia. The high iron values in the deteriorated group seem to reflect a general lowering of oxidative processes in these patients with far advanced schizophrenia.

Little is known about the brain metabolism or tissue iron content in the conditions in our miscellaneous group. It may be noted, however, that the iron values were high in five of the seven depressed patients and low in the two manic patients. The number of patients who were examined before and after electric convulsion and malaria fever therapy is too small to suggest a definite trend of the spinal fluid iron level in response to these treatments.

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25. Katzenelbogen, S.; Haws, R. J., and Snyder, R.: Biochemical Studies on Patients with Schizophrenia: Dextrose, Oxygen and Carbon Dioxide Contents of Arterial and Venous Blood from Cranial Cavity, Arch. Neurol. & Psychiat. **51**:499-471 (May) 1944.

SUMMARY

1. The iron content of the cerebrospinal fluid of 98 patients committed to a hospital for mental disease is examined.

2. The relation of the iron content of the brain to that of the spinal fluid is discussed.

3. When the patients were divided into various diagnostic groups, a statistically significant difference between the spinal fluid iron of the acute and that of the deteriorated schizophrenic patients appeared. The difference between the spinal fluid iron of the group with organic psychoses and that of the group with acute schizophrenia was very significant.

4. It is assumed that a low iron content of the spinal fluid is indicative of increased brain metabolism and that high iron values of the spinal fluid may reflect reduced cellular activity of the brain tissue.

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THE PALMOMENTAL REFLEX

A Physiological and Clinical Analysis

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THE PALMOMENTAL reflex, first described 30 years ago by Marinesco and Radovici,[1] is a fleeting unilateral contraction of the chin muscle on stimulation of the thenar eminence of the ipsilateral hand. It has received only cursory attention except in the Continental literature. Its reported incidence in the normal adult population has ranged from zero to 58 per cent; most observers have found it with greater frequency in infants. Its pathway has not been defined, and no agreement has been reached concerning its clinical significance.

For these reasons, a new study of this curious reflex was projected, aimed at (1) an analysis of its mechanism, variability and modifying factors and (2) a reappraisal of its clinical value.

HISTORICAL REVIEW

The reflex was discovered by Marinesco and Radovici in a patient with amyotrophic lateral sclerosis with extensive involvement of the corticobulbar tracts.[2] These investigators found the reflex in almost 50 per cent of normal adults and in 74 per cent of children less than 1 month of age. It was more frequently present in patients with "pyramidal" lesions, and in such instances the response was more pronounced and sustained on the weaker side. It was further noted that the reflexogenous zone normally did not extend beyond the palm, that the platysma sometimes participated in the reflex contraction and that the reaction was abolished in progressive bulbar paralysis and other lesions of the facial nucleus or nerve. The authors commented on the unusual features of the reflex—the distance from stimulus to response and the paradoxical exaggeration of this apparently superficial reflex in patients with supranuclear lesions.

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Presented at the Seventy-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 12, 1950.

1. Marinesco, G., and Radovici, A.: Sur un réflexe cutané nouveau: réflexe palmomentonnier, Rev. neurol. **27**:237, 1920.

2. The term "corticobulbar" is here used in its current sense to denote the projection fibers which connect the cerebral cortex with cranial nerve motor neurons in the brain stem. The related term "corticospinal" refers to similar motor fibers connecting with anterior horn cells in the cord. The older term, "pyramidal," as found in the references cited, refers in some instances merely to these fibers but is often more inclusive, for the pyramidal tracts are composed of fibers of wide, and in part uncertain, origins. To indicate the doubts which exist concerning the exact extent of many of the "pyramidal" lesions cited, this term will be enclosed in quotes.

Herscovici,[3] examining the reflex in normal infants up to 1 year of age, confirmed its higher incidence in early life and attributed this to delayed myelination of corticobulbar fibers, an explanation which (applied to corticospinal fibers) has been offered also for the Babinski response in infants. In additional studies on this reflex, Radovici [4] was apparently the first to comment on the possible significance of the proximity of the hand and face areas in cortical topography. It was found that old age per se had no effect on the incidence of the reflex.[5]

Juster [6] stressed the difference between the normal (fleeting) and pathological (sustained) responses and noted occasional extension of the reflexogenous zone to the arm and chest when the response was exaggerated. Sarno [7] found a lower incidence among normal subjects than had previous investigators; he reported a high incidence with hemiplegia and parkinsonism. On the other hand, Díaz,[8] in a survey of normal subjects and patients with "pyramidal" and extrapyramidal disease, concluded that the palmomental reflex was of no diagnostic value. Rusinowa [9] studied 550 patients with neurological disease, as well as 300 healthy persons, and concluded that the presence of the reflex had no great diagnostic importance, although its exaggeration denoted diffuse cerebral damage. Schachter [10] examined a large series of children aged 6 to 12 years, but came to no definite conclusions regarding the significance of the reflex. Thompson [11] considered the reflex diagnostic of dementia paralytica. Elsewhere in the literature the reflex is given only passing, and sometimes inaccurate, mention.[12] Some of the earlier

3. Herscovici, H.: Le réflexe palmo-mentonnier chez le nouveau-né, Spitalul, 1920.

4. Radovici, A.: (*a*) La sémiologie du réflexe palmo-mentonnier, Ann. de méd. **12**:56, 1922; (*b*) Un nouveau signe de diagnostic de la paralysie faciale: l'abolition du réflexe palmo-mentionnier (Marinesco-Radovici), Presse méd. **34**:453, 1926.

5. Radovici, A; Schachter, M., and Cohen, E.: Le réflexe palmo-mentonnier chez les vieillards, Bull. Soc. roumaine neurol., psychiat., psychol. et endocrinol., 1933, no 5, p. 187.

6. Juster, E.: Les réflexes cutanés palmaires, Rev. neurol. **31**(pt. 1):807, 1924.

7. Sarno, D.: Sul riflesso palmo-mentoniero, Neurologica **3**:321, 1926.

8. Díaz, J. M.: Semiología del reflejo palmo-mentoniano de Marinesco y Radovici, An. de med. int. **2**:281, 1933.

9. Rusinowa, J. G.: The Symptom of Marinesco-Radovici and Its Importance for the Clinic (in Russian), Sovet. psikhonevrol. **10**:59, 1934.

10. Schachter, M.: Le réflexe palmo-mentonnier (Marinesco-Radovici) chez l'enfant, Rev. franç. de pédiat. **13**:180, 1937.

11. Thompson, G. N.: The Palmo-Mental Sign, Bull. Los Angeles Neurol. Soc. **10**:174, 1945.

12. (*a*) de Castro, A.: Le réflexe cutané du menton, Rev. neurol. **1**:15, 1926. (*b*) Cornil, L.: Le réflexe linguo-mentonnier, Compt. rend. Soc. de biol. **95**:1491, 1926. (*c*) Sanchís Banús, J.: Libro homenaje a Marañón, Madrid, Paracelso, 1929. (*d*) Russetzki, J.: Le syndrome pyramidal, Acta med. Scandinav. **73**:260, 1930. (*e*) Epstein, A. L.: Somatologische Studien zur Psychiatrie, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:124, 1932. (*f*) Moldaver, J.: Étude de la courbe de sommation centrale du réflexe palmo-mentonnier de l'homme, Compt. rend. Soc. de biol. **109**:1143, 1932. (*g*) Magnusson, J. H., and Wernstedt, W.: The Infantile Palmo-Mentalis Reflex, Acta pædiat. (supp. 1) **17**:241, 1935. (*h*) Michon, P., and Adam, J. P.: Syndrome pyramidal au membre supérieur, Rev. méd. de Nancy **67**:137, 1939. (*i*) Benedek, L., and von Angyal, L.: Über die palatomentalen und corneomentalen Reflexe, Ztschr. f. d. ges. Neurol. u. Psychiat. **172**:632, 1941. (*j*) Wechsler, I. S.: A Textbook of Clinical Neurology, with an Introduction to the History of Neurology, Philadelphia, W. B. Saunders Company, 1947, p. 19. (*k*) Wartenberg, R.: News and Comment, Bull. Los Angeles Neurol. Soc. **13**:179, 1948.

work [13] alluded to the significance of isochronism in the mechanism of the reflex, but this aspect no longer seems relevant.

The various reports of the incidence of the palmomental reflex in the normal population, recorded between 1920 and 1945, are summarized in table 1.

METHODS

Observations on the palmomental reflex were made on 170 normal adult subjects and 43 patients with structural diseases of the nervous system. Three lines of study were followed:

1. The characteristics of the normal reflex were noted.

2. Attempts were made to modify the response by selective blocking of the afferent pathways or by the induction of pain in or adjacent to the receptive area of the reflex.

3. An appraisal was made of the clinical significance of the reflex in neurological disease, extending the observations already recorded in the literature. No attempt was made at a systematic survey of large groups of patients; the results thus do not justify extensive statistical analysis or detailed conclusions.

TABLE 1.—*Reported Incidence of the Palmomental Reflex*

Observer and Year	Adults		Children Under 1 Yr.		Children 1-14 Yr. of Age	
	No.	Incidence	No.	Incidence	No.	Incidence
Marinesco and Radovici,[1] 1920	300	50%	31	74%	...	....
Herscovici,[2] 1920	...	....	120	75-90%	?	50%
de Castro,[12a] 1926	"Many"	"Rare"	...	....	...	....
Sarno,[7] 1926	100	8%	...	....	...	....
Epstein,[12c] 1932	?	"Rare"	...	....	...	....
Díaz,[8] 1933	208	11%	...	....	...	....
Radovici and others,[5] 1933	116	58%	...	....	...	....
Rusinowa,[9] 1934	...	....	"Absent in infants"		...	....
Magnusson and Wernstedt,[12g] 1935	60	"None"	469	0-73% *	400	4%
Schachter,[10] 1937	...	....	...	....	1207	28%
Thompson,[11] 1945	"Many"	2-3%	...	....	...	....

* An incidence of 73 per cent in the first month, falling to zero by the ninth month.

OBSERVATIONS

The Normal Palmomental Reflex.—It was observed that the optimal stimulus was a brisk stroke with a blunt point on the thenar area of the palm (fig. 1), applied with sufficient force to cause mild discomfort. A key was used as a convenient stimulator. The upward movement thus evoked in the ipsilateral mentalis muscle, innervated by the facial nerve, was slight, brisk and very brief (fig. 2). It varied in amplitude with the strength of the stimulus and was readily exhausted by stimuli repeated in close succession. Recovery of excitability occurred within a minute or less. When present, the reflex could usually be elicited from each hand; it was sometimes more pronounced on one side (usually the left), without relation to handedness. In this series the reflex was elicited in 49 per cent of 170 normal adults (from 20 to 60 years of age) and with few exceptions was bilateral.[14]

13. Radovici.[1a] Juster.[6] Cornil.[12b]

14. Incidental to the main study, it was noted that the palmomental reflex could not be elicited in any of four rhesus monkeys tested, perhaps in part because of the relatively underdeveloped chin muscles in this animal.

The intensity of the response varied within moderate limits from person to person and, within somewhat narrower limits, in the same person from day to day. Part of this variability could be attributed to minor differences in the stimulus, for the technic is not readily standardized. This factor may also be responsible

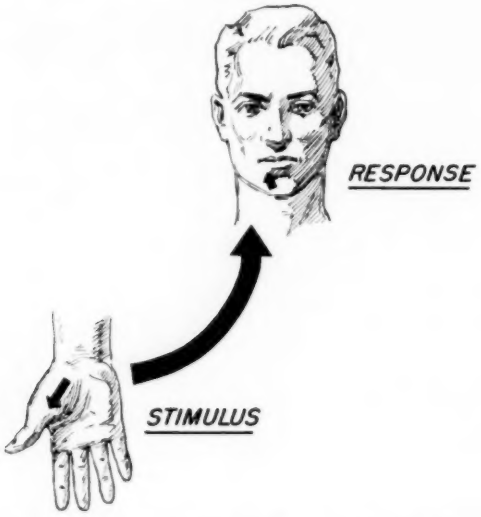

Fig. 1.—Diagram of the palmomental reflex, indicating the location and direction of the standard stimulus on the thenar eminence and the site and direction of the chin response.

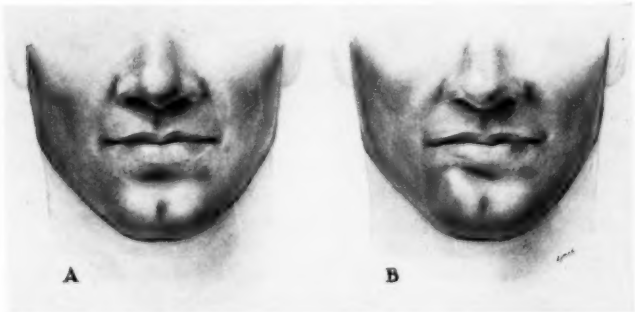

Fig. 2.—Sketch of a normal palmomental reflex response: (*A*) the chin at rest; (*B*) a contraction of the right mentalis muscle evoked by stimulation of the thenar area of the right palm. The change in contour of the chin is here slightly exaggerated by the artist for purposes of clarity.

for some of the discrepancies in the reported incidence of the reflex. The intensity of the response could not be correlated with that of other normal superficial or deep reflexes or with the presence of fatigue or emotional tension.

Attempts at Modification of the Reflex.—The reflex could be modified experimentally in various ways:

1. The response was abolished in each of two subjects by superficial procainization of the reflexogenous zone, leaving deep pain intact, as confirmed by probing the underlying muscles with a needle.

2. In six subjects (10 experiments) ischemia of the arm was induced by a cuff at the midhumerus level. The response in four of the subjects was reduced or abolished coincident with the onset of moderate impairment of "fast" conduction pain sensibility, despite the accompanying dysalgesia of "slow" condition pain induced by the stimulus. A representative experiment is summarized in figure 3. This effect was consistently demonstrated in each of four experiments on one of the subjects.

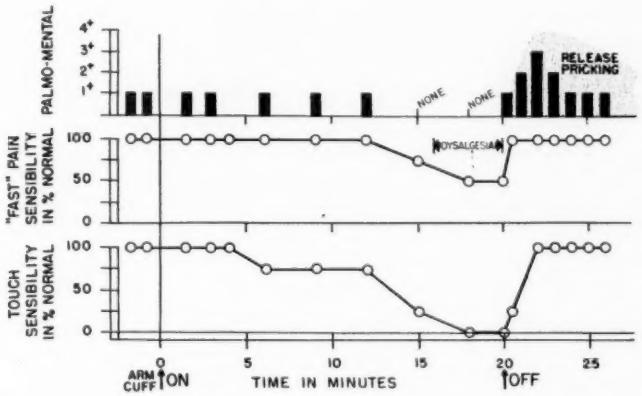

Fig. 3.—A representative experiment indicating the effect of ischemic block by a cuff about the upper arm in (*a*) diminishing the palmomental reflex during the phase of impairment of sensibility and (*b*) enhancing the response during the phase of "release pricking."

3. In contrast, the intensity of the response was increased in 10 of 13 subjects (17 experiments) during "release pricking" in the hand after prolonged cuff ischemia (fig. 3). This pricking paresthesia has been attributed by Weddell and Sinclair [15] to increased excitability of peripheral pain fibers, although more recent electrophysiological studies [16] suggest that other sensory pathways may be involved.

4. The response was also accentuated in one subject (three experiments) during painful galvanic stimulation of the thenar eminence directly adjacent to the site from which the reflex was elicited. This experiment was designed to ascertain

15. Weddell, G., and Sinclair, D. C.: "Pins and Needles": Observations on Some of the Sensations Aroused in a Limb by the Application of Pressure, J. Neurol., Neurosurg. & Psychiat. **10**:26, 1947.

16. Magladery, J. W.; McDougal, D. B., and Stoll, J. N.: Electrophysiological Studies of Nerve and Reflex Activity in Normal Man: III. The Post-Ischemic State, Bull. Johns Hopkins Hosp. **86**:313, 1950.

the effect of noxious impulses entering the central nervous system close to the afferent path of the reflex itself, since it has been shown that deep reflexes, at least, may be facilitated by such added central excitation.[17]

Comment: On the basis of these observations, and since the stimulus normally must be noxious to be effective, it is tentatively inferred that the afferent arc of the palmomental reflex is over superficial pain fibers. Furthermore, the latent period of the reflex, as determined by Golla and Antonovitch,[18] is short (0.05 second). This finding, together with the aforementioned observation that the response is reduced when "fast" pain sensibility is impaired by arm ischemia, suggests that the afferent pathway traverses fast conduction pain fibers. It may be relevant in this connection that in all of four patients with cervical syringomyelia, showing loss of superficial pain sensibility in the hands with little or no impairment of light touch, the reflex was absent.

In the light of this incomplete evidence that the palmomental reflex may be subserved by nociceptive fibers, it is of additional interest that Sarnoff and Arrowood,[19] employing differential spinal block, observed abolition of the superficial abdominal, patellar and achilles reflexes coincident with the loss of pinprick sensibility in the corresponding dermatomes; these phenomena occurred despite

TABLE 2.—*Incidence of Peripheral Facial Palsy*

Observer and Year	No. Patients Examined	Reflex Present on Affected Side	Reflex Present on Unaffected Side
Sarno,[7] 1926	5	0	1
Radovici,[4b] 1926	10	0	8
Present study, 1950	5	0	4

apparently full preservation of muscle power and touch, position and vibration sense. In only one of their subjects were the plantar and cremasteric reflexes tested during the block; these responses also were absent.[20]

The Reflex in Neurological Disease.—As indicated in table 2, in which the present observations are combined with those reported by others, in patients with lesions of the facial nerve or nucleus the palmomental reflex was unobtainable on the affected side.

In contrast, the response was present in high incidence in patients with disorders affecting suprasegmental motor pathways, confirming what most observers have reported with "pyramidal" disease (table 3). Furthermore, in the presence of such lesions, the response was commonly increased in intensity, as reported also by earlier investigators. When pathologically accentuated, the response sometimes

17. (*a*) Porter, E. L., and Taylor, A. N.: Facilitation of Flexion Reflex in Relation to Pain After Nerve Injuries (Causalgia), J. Neurophysiol. **8**:289, 1945. (*b*) Thompson, L., and Gellhorn, E.: Influence of Muscle Pain on Spinal Reflexes, Proc. Soc. Exper. Biol. & Med. **58**:105, 1945.

18. Golla, F., and Antonovitch, S.: A Note on the Palmar Chin Reflex of Marinesco, J. Ment. Sc. **80**:513, 1934.

19. Sarnoff, S. J., and Arrowood, J. G.: Differential Spinal Block: III. Block of Cutaneous and Stretch Reflexes in the Presence of Unimpaired Position Sense, J. Neurophysiol. **10**:205, 1947.

20. Arrowood, J. G.: Personal communication to the authors.

presented other unusual features: (*a*) It was deliberate in its rise and fall; (*b*) it spread to include the platysma on the same side; (*c*) it resisted exhaustion by repeated stimulation; (*d*) it had a wider receptive field, extending in some patients to include the anterior surface of the arm and chest, or (*e*) it could be elicited by a light stroke or by a single pinprick. Analogy to the behavior of the extensor plantar response is evident. According to the criteria set for the present study, a pathologically accentuated palmomental reflex was defined merely as one in which the movement of the mentalis muscle was greater in amplitude or more sustained or both than the response of this muscle in normal subjects. These distinctions can be based only on previous experience with the variability of the response among large numbers of normal subjects; even with this preparation a decision in some instances is difficult.

The accentuated reflex was frequently noted in patients with diverse forms of corticobulbospinal tract disease, especially when bilateral, e. g., cerebrovascular

TABLE 3.—*Lesions of "Pyramidal" Tract*

Observer and Year	No. Patients Examined	Reflex Present
Sarno, 1926	14	13
Radovici,[4b] 1926	15	11
Sanchís Banús,[12c] 1929	30	8
Díaz,[8] 1933	27	15
Radovici and others,[5] 1933	30	24
Present study, 1950	24	20

TABLE 4.—*Parkinsonism*

Observer and Year	No. Patients Examined	Reflex Present
Sarno, 1926	10	10
Sanchís Banús,[12c] 1929	"Many"	(90%)
Díaz,[8] 1933	22	15
Radovici-Schachter-Cohen,[5] 1933	6	5
Present study, 1950	4	3

accidents (eight of 10 patients), cerebral tumors (six of seven patients), amyotrophic lateral sclerosis (three of four patients), multiple sclerosis (one of two patients) and dementia paralytica (1 patient). The reflex was found, on the weaker side at least, in 15 of 17 patients with hemiplegia due to intracranial lesions of varied types, and in 12 of these it was accentuated; yet in three of the 12 patients no facial weakness was detectable. Thus, an abnormally active palmomental reflex can occur without frank involvement of corticofacial fibers, although in this series the response was more consistently accentuated when facial weakness was apparent. No difference was noted in the effects on the reflex of cortical and of internal capsular lesion.

In parkinsonism, with which the reflex has been found by others in high incidence (table 4), a response was noted in three of four patients, in two of whom it was exaggerated. The anatomic significance of this association is conjectural, for the mechanism of parkinsonism remains incompletely defined. This extrapyramidal disorder is here included as a separate, and unusually complex, type of suprasegmental motor disease.

Of incidental interest were the following findings in certain disorders:

1. In the one of the four patients with amyotrophic lateral sclerosis in whom the palmomental reflex was absent, advanced bulbar (lower motor neuron) disease was evident.

2. In three patients with extensive traumatic injuries to the high cervical portion of the cord, the reflex was absent.

3. In a patient with a severe injury to the left brachial plexus, resulting in flaccid paralysis of the arm and loss of all sensation over the fifth to the eighth cervical dermatome, no response could be elicited from the anesthetic hand, but a normal reflex was found on the right.

4. In a patient with a ruptured cervical intervertebral disk, resulting in unilateral hypesthesia and hypalgesia over the sixth and seventh cervical dermatomes, the response was diminished on the affected side.

5. In a patient with severance of the median and ulnar nerves and clearly circumscribed sensory loss involving part of the thenar eminence, the reflex was absent when the anesthetic thenar area was stimulated but could be elicited from the adjacent thenar border, supplied by the intact radial nerve. Thus, the receptive field for the reflex is principally, but not entirely, in the domain of the median nerve.

COMMENT

The Reflex Pathway.—The complete pathway of the reflex is uncertain, but the experimental observations indicate that fast conduction pain fibers constitute the afferent arc. In spite of the suggestive proximity of the hand and face areas in cortical sequence, it is unlikely that the precentral motor strip (area 4) is directly involved, for the reflex response is enhanced by lesions of the corticobulbospinal tract. The efferent arc is clearly over the facial nerve.

It is possible that the reflex is purely intersegmental. This hypothesis, it will be noted, requires the assumption that impulses passing up in the spinothalamic tract cross back below or in the medulla or that some nociceptive fibers ascend uncrossed, at least as far as the facial nucleus. Evidence for the second possibility has recently been reported.[21]

The Essential Nature of the Reflex.—The observations here presented indicate that the palmomental reflex, a normal reflex, is frequently, but unpredictably, accentuated when released from suprasegmental control. Its inconsistency in neurological disease remains unexplained, probably in part because the extent of the brain lesions in the studied cases is known only by inference, and therefore incompletely. The full usefulness of the reflex cannot be defined until accurate correlations are made of the clinical and the pathological data. Such a combined antemortem and postmortem study would be feasible only if testing of the reflex were to become routine—an unlikely development.

This much, however, is clear: In spite of its status as a superficial reflex, the palmomental reflex acts in one respect as do deep reflexes; i. e., it is commonly exaggerated with corticobulbospinal tract disease. Because of this

21. Sweet, W. H.; White, J. C.; Selverstone, B., and Nilges, R.: Sensory Responses from Anterior Roots and from Surface and Interior of Spinal Cord in Man, Tr. Am. Neurol. A. **75**:165, 1950.

paradoxical behavior and the absence of the reflex in many normal subjects, the palmomental response occupies a special position among human reflexes. It is also unique in the remarkable intersegmental distance which normally separates stimulus from response (sixth cervical segment to the seventh cranial nerve). As Wartenberg has emphasized, certain superficial reflexes, such as the abdominal or the plantar, can sometimes be elicited from relatively remote body areas, but in all such reflexes the response is still more readily evoked by local (intrasegmental) stimulation.[22]

The "primitive meaning" of the palmomental reflex is obscure. The mode of elicitation and the pattern of the response suggest a fragmentary "wince" reaction. If this formulation is valid, the accentuation of the reflex when separated from higher centers may be analogous to the exaggeration of emotional facial movements sometimes noted under similar circumstances.[23] As Thompson [11] has already noted in discussing the nature of the palmomental reflex, the chin muscles play a prominent role in the expression of discomfort. It seems particularly relevant that quivering of the chin commonly precedes or replaces an outburst of weeping.[24]

Its Clinical Value.—The diagnostic value of the palmomental reflex is restricted by its vagaries. Yet the test is easily and rapidly done and can at once alert the examiner to the presence of structural brain disease. Although a hyperactive response often indicates a suprasegmental motor lesion, absence of the reflex does not rule out such disease. The presence or accentuation of the response may sometimes be of specific diagnostic aid; for example, it may distinguish central from peripheral facial paralysis, or amyotrophic lateral sclerosis from tumor of the high cervical portion of the cord, and it may be the only obvious clue to an old cerebrovascular accident.

SUMMARY AND CONCLUSIONS

The palmomental reflex, found in one-half the normal adult population, presents a remarkable distance from receptive field to area of response. From experimental analysis of its mechanism, it is tentatively inferred that the afferent arc employs superficial fast conduction pain fibers. The pattern of the response suggests a fragmentary wince. As has been reported by other investigators in the past 30 years, the reflex is commonly, but not predictably, accentuated on release from cortical control.

The reflex has limited clinical value, but when exaggerated it is a useful alerting sign of suprasegmental motor disease.

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22. Wartenberg, R.: The Examination of Reflexes: A Simplification, Chicago, The Year Book Publishers, Inc., 1945.

23. Monrad-Krohn, G. H.: Dissociation of Voluntary and Emotional Innervation in Facial Paresis of Central Origin, Brain **47**:22, 1924.

24. Somewhat comparable is the observation of Charles Darwin: "I believe that the depressor muscles of the angles of the mouth are less under the separate control of the will than the adjoining muscles, so that if a young child is only doubtfully inclined to cry, this muscle is generally the first to contract and is the last to cease contracting" (The Expression of the Emotions in Man and Animals, New York, D. Appleton and Co., 1897, p. 150).

OCCLUSION OF THE INTERNAL CAROTID ARTERY

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SINCE the introduction of carotid arteriography, many unsuspected cases of occlusion of the internal carotid artery have been discovered. In the last 13 years approximately 45 cases have been reported, the diagnosis resting to a great extent on roentgenologic evidence. Recent clinical and pathological studies have led me to the conclusion that thrombosis of the internal carotid artery is much more frequent than these figures indicate. Indeed, it may well prove to be one of the major causes of apoplexy. This impression is confirmed by Hultquist,[1] who, in his extremely thorough study of the pathological aspects of this subject, found thromboembolism of the carotid system in about 3 per cent of routine autopsies. Clinicians and pathologists have heretofore failed to appreciate this condition, because the cervical portion of the carotid artery lies in a "no-man's land" between general pathology and neuropathology, its examination at autopsy being therefore neglected. Chiari,[2] and later Hunt,[3] emphasized investigation of the carotid vessels in the neck in all cases of apoplexy, but their advice has been disregarded.

My interest in this subject was aroused while working in the Mallory Institute of Pathology, under the direction of Dr. Raymond D. Adams. There, in case after case, neuropathological examination failed to confirm the clinical impression of disease of the middle cerebral artery. During a period of nine months, in which the brains in 200 cases of cerebrovascular disease were examined, not a single case of thrombosis of the middle cerebral artery was found, although the diagnosis had often been made clinically. It was logical to look more proximally, namely, in the internal carotid artery, for unrecognized disease. Moreover, during our study of brain embolism,[4] in many cases no source for the embolus could be found in the conventional locations—the pulmonary veins, the left auricle, the left ventricle or the ascending aorta. The neglected area, again, seemed to lie in the carotid system, which we did not investigate by direct visual inspection at autopsy, only testing its

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1. Hultquist, G. T.: Über Thrombose und Embolie der Arteria carotis und hierbei vorkommende Gehirnstörungen, Jena, Gustav Fischer, 1942.

2. Chiari, H.: Über das Verhalten des Teilungswinkels der Carotis communis bei der Endarteriitis chronica deformans, Verhandl. d. deutsch. path. Gesellsch. **9**:326, 1905.

3. Hunt, J. R.: The Role of the Carotid Arteries, in the Causation of Vascular Lesions of the Brain, with Remarks on Certain Special Features of the Symptomatology, Am. J. M. Sc. **147**:704, 1914.

4. Fisher, M., and Adams, R. D.: To be published.

patency to injected fluids. A methodical search for disease of the internal carotid artery at necropsy was therefore undertaken and has been surprisingly rewarding. Likewise, many cases are being found in the wards.

The present study deals with eight cases of occlusion of the internal carotid artery, four of which have been verified by postmortem examination. In two cases arteriographic or surgical confirmation of the diagnosis has been made, while in the remaining two cases the diagnosis was made clinically. All the patients have been seen on the wards of two general hospitals within a period of six months, and the cases are presented because it is believed that regular investigation of the internal carotid artery will reveal pathological processes which are among the most important causes of hemiplegia. Moreover, study of this syndrome will furnish

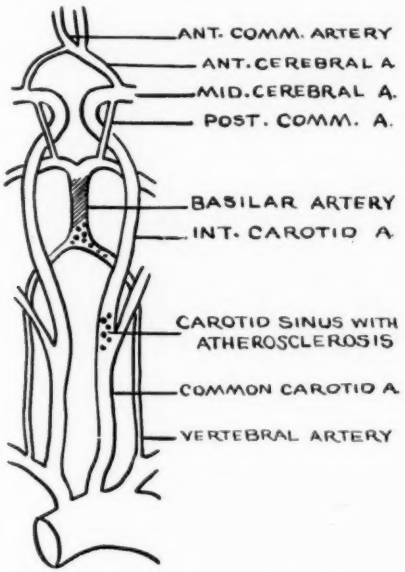

Fig. 1 (case 1).—The cerebral blood supply shown diagrammatically. The dotted areas represent atherosclerosis; the lined areas, recent blood clot. The circle of Willis is drawn in its true proportions.

important clues to the mechanism of many heretofore puzzling cerebral symptoms, especially transient episodes of blindness, aphasia, paresthesia and paralysis, as well as headache and dizziness.

ANATOMIC CONSIDERATIONS

Figure 1 shows the cerebral blood supply diagramatically. There are four main arteries of supply, two internal carotid and two vertebral arteries. Since the two vertebral arteries become one, the basilar artery, the main arteries may be considered as three. The common carotid artery arises from the innominate artery on the right and from the arch of the aorta on the left. At the level of the thyroid cartilage it divides into the external carotid and the internal carotid artery. The

former soon divides into its superior thyroid, lingual, occipital, maxillary and temporal branches. The internal carotid artery pursues its upward course, through the petrous process of the temporal bone and the cavernous sinus. As it emerges upward out of the sinus, it gives off the ophthalmic artery, and soon thereafter the posterior communicating artery, which runs posteriorly to the posterior cerebral artery of the same side. Almost immediately it divides into the anterior and the middle cerebral artery.

The anterior cerebral arteries on the two sides are connected by the anterior communicating artery, which completes the circle of Willis anteriorly. The two posterior cerebral arteries complete the circle of Willis posteriorly. The size of each of these component arteries is highly variable and determines the adequacy of collateral circulation from one side to the other, as well as between the basilar and the carotid systems. In some cases there are probably small arteries on the surfaces of the hemispheres which provide important connections between the anterior, middle and posterior cerebral arteries.

REPORT OF CASES

CASE 1.—*History.*—A man aged 64 complained of transient attacks characterized by dizziness, inability to speak and paralysis and numbness of the right hand. He said he had had at least 100 attacks in eight months. His family confirmed this statement, although he had tended not to acquaint them with his complaints. All the attacks were similar but varied in duration and severity. They usually began with a severe pounding sensation behind the left ear. Next there appeared a steady headache over the left eye. Then severe rotatory dizziness (clockwise) began, causing him to sweat and become nauseated, sometimes to the point of vomiting. During the vertigo, diplopia occurred, one image lying directly above the other. At the same time, the right hand became numb and paralyzed, and he was unable to speak a word, although he knew what he wanted to say. He retained complete awareness. A short attack lasted 15 minutes; a "long one" would take 40 minutes to clear. The headache usually persisted throughout the attack and for a short while afterward. During the attack the temporal vessels on the left side pulsated prominently. On one occasion an attack began when he was driving his car in heavy traffic. He immediately stopped the motor and, being unable to speak, sat by, while a traffic officer steered his car to the curb. A few minutes later he was allowed to drive on home. The attacks were gradually becoming more frequent and more severe as the months passed. However, between attacks he felt perfectly well, worked regularly and remained mentally keen. Vision in the left eye was never affected.

Three days before admission, he suddenly lost consciousness for 40 minutes and, on recovering, found he had a severe left hemiplegia, which cleared in about six hours. He had never lost consciousness previously, nor had the left side been affected. During the two days before admission he had had several recurrences of his attacks involving the right side.

On admission he was clear mentally and gave a detailed history. Speech was definitely slurred, but he had had an attack shortly before examination. The pupils were equal and reacted to light and in accommodation. The visual fields were full. Ocular movements were unrestricted, but a nystagmoid jerking on lateral gaze was so pronounced as to be suspected of being abnormal. The fundi were normal except for irregularity and widening of the arterial light reflex. There was no facial weakness. He swallowed normally. Auditory acuity was decreased in the right ear, but he had been partially deaf in that ear since the age of 17. Bone conduction was better than air conduction bilaterally, and hearing in the Weber test was referred to the left. Motor power and coordination of the limbs were good. Careful sensory examination showed no deficit. The deep reflexes were equal on the two sides. The plantar response was promptly elicited on the right, while there was little response on the left. The right sole was more ticklish than the left. Pulsation in the left carotid artery was much less forceful than in the right. No bruit could be heard over the skull or over the carotid vessels.

The heart appeared slightly enlarged clinically. The sinus rhythm was normal. The blood pressure was 240/110. Pulsation was absent in the right posterior tibial artery. There was no laboratory evidence of diabetes mellitus or anemia.

During the patient's first two days in the hospital, at least four transitory attacks of speechlessness and complete paralysis of the right arm occurred. He was examined during one of these episodes and was found to be unable to speak, although he carried out commands with the left hand. Consciousness was not impaired, for later he could recall the various tests he had been asked to perform during the attack. The Babinski sign appeared on the right. Recovery of power in the right hand began to occur in 20 minutes. Speech reappeared at the same time, and no period of dysphasia was noted.

On the third hospital day, at 2 p. m., he complained of pounding behind his left ear. At 2:30 p. m. he had a severe shaking chill, lasting about one-half hour, and afterward he vomited. At 3:30 p. m. he suddenly became deeply unconscious, with jerking of the limbs and stertorous respiration, but after a few minutes recovered sufficiently for it to be recognized that a massive left hemiplegia was present. He soon became deeply comatose again, with rapid Cheyne-Stokes respiration. Pulmonary edema appeared. He died five hours later, and during the interval

Fig. 2 (case 1).—Cervical portion of the carotid arteries. The left carotid sinus is shown in cross section.

many attacks of dancing nystagmus occurred, the eyeballs darting and shaking, although maintained in a relatively central position.

The clinical diagnosis of bilateral occlusion of the internal carotid artery was only partially confirmed at necropsy.

Anatomic Diagnoses.—The diagnoses were atherosclerotic occlusion of the left internal carotid artery within the carotid sinus; thrombosis of the basilar artery; encephalomalacia, involving the right calcarine area and the right thalamus; cardiomegaly; severe atherosclerosis of the aorta and iliac arteries (the right iliac artery was almost occluded), and chronic interstitial nephritis (granular kidneys).

Neuropathological Study.—The only superficial abnormality of the brain was a yellowish gray focus, 4 cm. in diameter, of recent softening in the cortex of the right occipital lobe, in the territory of the calcarine artery. Section revealed a small, pale softening in the medial portion of the right thalamus. The circle of Willis had a large anterior communicating artery (3 mm. in diameter), a small right posterior communicating artery (0.75 mm.) and a good-

sized left posterior communicating artery (1.5 mm.). There was extensive atherosclerosis of the cerebral arteries. The left vertebral artery was entirely occluded, and the inferior portion of the basilar artery was narrowed to two 0.5 mm. holes, both blocked by red clot.

Both carotid systems were examined their entire length. The left internal carotid artery, in the region of the carotid sinus, was narrowed to a slit about 1 mm. in width by a mass of yellow tissue (figs. 1 and 2). The right carotid sinus showed very little atherosclerosis. The portion of the right internal carotid artery within the skull had several plaques of atherosclerosis, but the lumen was not severely narrowed.

Histological study revealed the occluding masses in the left internal carotid artery and the left vertebral artery to be atherosclerotic. The basilar artery was occluded by atherosclerotic tissue, with a superimposed recent antemortem thrombus.

Summary.—This patient had repeated transient episodes of vertigo, diplopia, paralysis of the right hand and aphasia. Finally, two attacks occurred on the left side, in the second of which he died. The left internal carotid artery was almost entirely occluded in the region of the sinus by an atherosclerotic mass. The right internal carotid artery was patent. The inferior portion of the basilar artery was narrowed to a slit by atherosclerotic plaques. The pathogenesis of all the symptoms is not definite, but it is likely that the right internal carotid artery carried the main blood supply to the brain and brain stem. Intermittent closure of the left internal carotid artery caused temporary ischemia of structures supplied by the basilar system sufficient to produce dizziness and diplopia, at the same time as the reduced flow in the territory of the middle cerebral artery caused paralysis and aphasia. There is the possibility that the vertigo arose from a disorder of the cerebral cortex, in which case it need not be assumed that intermittent closure of the internal carotid artery influenced the flow in the basilar system. Thrombosis of the basilar artery was probably the immediate cause of death, an antemortem clot blocking the lower half of the basilar artery. There were no lesions in the left cerebral hemisphere.

Case 2.—A man aged 68 had had a paralytic stroke on the left side in June 1947, about three years before his death. Early one morning his wife found him struggling to get out of bed, and it was apparent that he had a severe left hemiplegia. He was not unconscious, but for several months was confused, forgetful and incontinent of urine.

During the two months before the onset of hemiplegia, on five or six occasions, he had had transient blindness of the right eye, lasting about three minutes. He was examined by an ophthalmologist, but nothing remarkable was found. He was quite certain that he was blind in only one eye and said that it was as though a blind had been pulled down. During the same period he had frequently remarked to his wife, "I don't seem to have much feeling in my fingers" (left hand). The attack would pass off shortly. He did not have dizziness or headache.

There was very little recovery from the paralysis, and when he was examined two and a half years later he could walk only very slowly, using a cane. There was weakness of the left side of the face. The left hand was completely immobile. The left leg was extremely spastic. The tendon reflexes were brisker on the left side, and two point discrimination was impaired on this side. The visual fields were full. The fundi were not remarkable. Careful estimation of the pulsation in the carotid arteries was made, and no difference between the two sides was detected. The blood pressure was 160/90. The arterial pulsations were normal in the lower extremities. The Wassermann reaction of the blood was negative. There was no evidence of diabetes mellitus or anemia.

The patient said that his mental condition had changed slightly, but definitely. His memory remained good, for he followed several sports closely and could recall all the details. However, his reading habits had degenerated to 25 cent magazines, whereas before his stroke he would not have "touched such junk with a 10 foot pole." At one time in his career he had been so

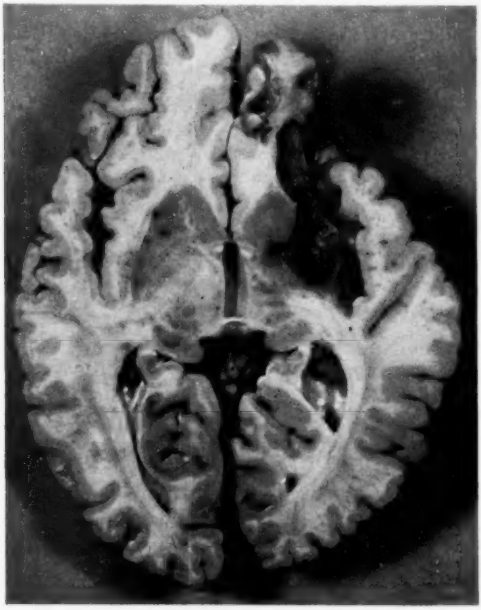

Fig. 3 (case 2).—Horizontal section of the brain. The frontal lobe, insula and lenticular nucleus on the right side have been destroyed.

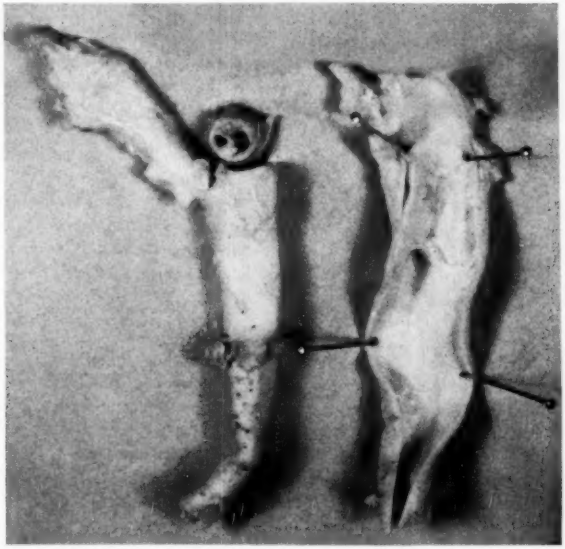

Fig. 4 (case 2).—The carotid arteries. The right carotid sinus is seen in cross section. The left carotid sinus has minimal atherosclerosis.

worried about having heart trouble that he gave up a good job as a civil engineer to become a clerk in an office. With the stroke he had lost this tendency to be nervous.

The patient's final illness was carcinoma of the rectum, for which an abdominoperineal resection was performed on June 16, 1950. Circulatory collapse followed the operation, and he died three hours later. Necropsy was performed.

Pathological Diagnoses.—The diagnoses were atherosclerotic occlusion of the right internal carotid artery within the carotid sinus; old area of encephalomalacia in the right frontal region; recent abdominoperineal resection wound, and metastatic carcinoma of the liver.

Neuropathological Study.—Inspection of the brain showed an extensive sunken region of old destruction involving the anterior four fifths of the frontal lobe, the insula and the outer portion

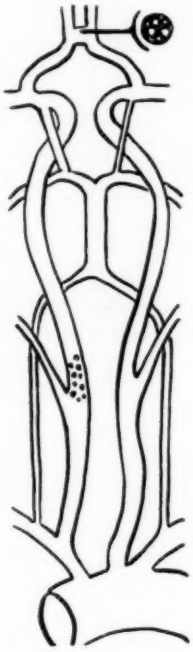

Fig. 5 (case 2).—Diagram of cerebral arteries, showing region of block. The anterior communicating artery is anomalous, within.

of the lentiform nucleus (fig. 3). The yellowish orange walls of this excavation were covered by thickened, gray pia-arachnoid. More posteriorly, there were isolated softenings in the superior parietal lobule and the angular gyrus. The cerebrospinal bundle in the brain stem was atrophic. The temporal lobe and most of the parietal lobe were normal.

The circle of Willis had small posterior communicating arteries and what at first appeared to be a large anterior communicating artery, which should have provided an adequate collateral blood supply. However, on section of the anterior communicating artery it was found that the lumen was not a single large space but consisted of three or four smaller vessels, whose walls occupied most of the lumen. The anterior communicating artery was, therefore, not of adequate size, in spite of its apparent large caliber as seen externally.

The right carotid sinus was firm, and on section its lumen was seen to be almost entirely obliterated by yellowish tissue, containing scattered red islands (figs. 4 and 5). The lumen was

about 1 mm. in diameter just above the bifurcation. This abnormality was limited to the region of the sinus, the internal carotid artery above being normal. The common carotid and external carotid arteries were almost free of atherosclerosis. The left carotid sinus had a 1 mm. layer of subintimal thickening, but the lumen was not seriously narrowed. The cerebral vessels showed only a few small atherosclerotic plaques.

Microscopically, the occluding tissue was for the most part dense collagenous connective tissue, but in the deeper portion there was atheromatous material. Recanalization or formation of small endothelium-lined channels had occurred in several places. There was no evidence of inflammation.

Summary.—This patient had an attack of severe hemiplegia three years before his death. For two months before the onset he had had several attacks of unilateral blindness and a "dead" feeling in the left hand. Pathological studies showed occlusion with recanalization of the right internal carotid artery in the region of the sinus. There was an area of old cystic encephalomalacia in the territory of the anterior and middle cerebral arteries. There was little intracranial atherosclerosis, and if the carotid vessels had not been examined the diagnosis would have remained obscure. The anterior communicating artery, although apparently large, proved to be inadequate, due to trabeculae within.

CASE 3.—A man aged 67 had two serious diseases: (1) Epidermoid carcinoma of the nasopharynx with metastases in the cervical region bilaterally. The swellings in the neck first appeared one and a half years prior to operation. He had had roentgen therapy and was admitted for resection of the lymph nodes in the right cervical area. (2) Coronary atherosclerosis with associated auricular fibrillation, cardiomegaly and pronounced electrocardiographic abnormality. In February 1950 the patient had been admitted to the hospital with moderate congestive cardiac failure, which had cleared in a few weeks.

The patient was admitted to a surgical service on May 17, 1950. There was no evidence of cardiac failure. Normal sinus rhythm had returned. The blood pressure was 130/90. He was clear mentally, and the neurological status was normal. There was a firm mass, about 4 cm. in diameter, in the right cervical region.

A radical neck dissection was performed on the right side. During the operation the common carotid artery was "obviously somewhat in spasm at times," but the branches of the external carotid artery continued to pulsate normally. The patient required assistant respiratory measures throughout the procedure. One hour after operation, vascular collapse occurred, and the systolic blood pressure fell to about 70 mm. for one and one-half hours. With restorative measures the blood pressure returned to preoperative levels, but eight hours after operation it was noted that he had left hemiparesis. He soon became restless and confused. Auricular fibrillation had reappeared. Twelve hours later he was comatose, the pupils did not react to light and there was severe flaccid hemiplegia of the left side. The pulsation of the carotid artery was not examined because of the neck bandages. One observer reported that vision was present in the right eye.

Heparin therapy was begun, but during the next 12 hours the patient became deeply comatose and Cheyne-Stokes respiration appeared. The right pupil dilated and became fixed to light. The patient died 72 hours after operation.

The clinical diagnosis rested between cerebral embolism and thrombosis of the right internal carotid artery.

Pathological Diagnoses.—Autopsy revealed atherosclerotic narrowing (extreme) of the right internal carotid artery in the region of the carotid sinus; recent thrombosis of the right internal carotid artery; encephalomalacia of the right cerebral hemisphere; carcinoma of the nasopharynx with metastases in the cervical glands; old myocardial infarction, and pulmonary congestion.

Neuropathological Study.—The right cerebral hemisphere in the territory of the anterior and middle cerebral arteries was soft, swollen and discolored (fig. 6). The territory of the

posterior cerebral artery was spared. A large transtentorial herniation of the temporal lobe was present on the right side. Extensive hemorrhages had occurred in the midbrain. There were no other lesions.

The circle of Willis showed a very small anterior communicating artery, and the posterior communicating vessels were small in comparison with the posterior cerebral arteries. The right internal carotid artery was tightly packed, with a dark red clot extending distally into the middle and anterior cerebral arteries and proximally to the region of the carotid sinus (fig. 7). At the sinus, the right internal carotid artery was narrowed by a white, firm atherosclerotic deposition, so that the diameter of the lumen was at one place no greater than 0.5 mm. (fig. 8). The cervical portion of the internal carotid artery was otherwise entirely free from atherosclerosis. There was no embolus proximal to the sinus.

Microscopic sections of the narrowed portions of the carotid sinus showed the plaque to be composed of abundant fibrous connective tissue containing atheroma and cholesterol crystals.

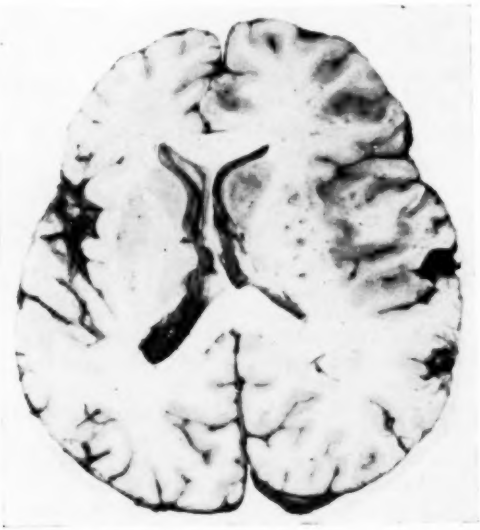

Fig. 6 (case 3).—Cross section of the brain. Note the swollen right hemisphere and the indistinct cortex.

There was no inflammation. The deposition was believed to be an atherosclerotic plaque, rather than an organized thrombus.

Summary.—This case is one of hemiplegia following a serious surgical procedure, complicated by shock and hypotension. Pathological examination showed almost complete atherosclerotic closure of the right internal carotid artery and, above this, an extensive fresh antemortem thrombus, obviously the cause of the cerebral lesion. The circle of Willis showed inadequate collateral channels. Again, in this case, if the internal carotid artery had not been examined in the neck, the cause of the hemiplegia would not have been apparent.

Case 4.—A man aged 54, in 1942, eight years before his death, had a mastoidectomy (left), the circumstances of which are not clear. After the operation he began to have periodic excruciating headaches on the right side. These were situated over the right eye, which became red and tearful during the attack. The headache lasted about one-half hour and occurred approximately once a week.

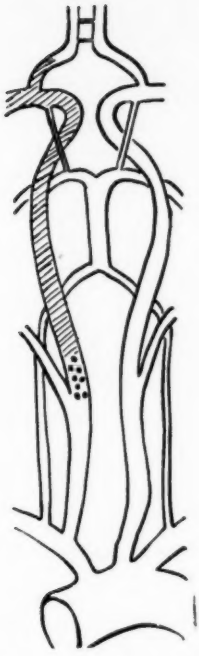

Fig. 7 (case 3).—Diagram of cerebral arteries. An extensive blood clot fills the right internal carotid artery, distal to an area of atherosclerotic narrowing.

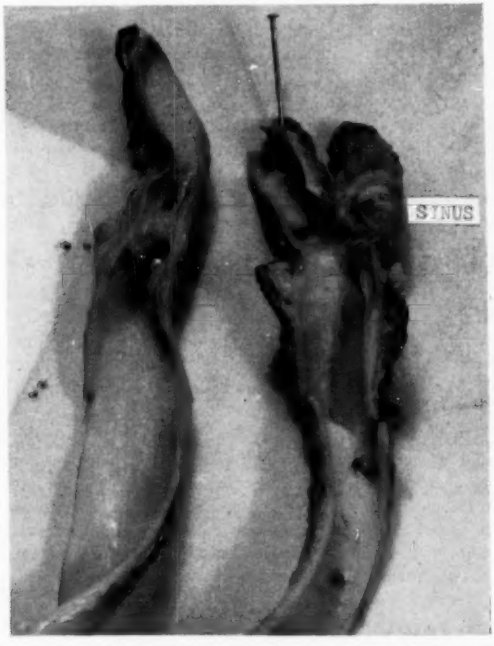

Fig. 8 (case 3).—The carotid arteries. The right carotid sinus is almost solidly occluded.

One morning in May 1943 the patient was difficult to awaken. He complained of severe headache and of feeling tired, and his face was unduly red. At 5 p. m. he complained of feeling dizzy, and his countenance was dark red. At 7:30 p. m., within one minute, he became very weak on the left side and for a short time was unable to speak. Within an hour severe left hemiplegia had developed, but speech had returned. He was right handed, and his speechlessness was probably a temporary anarthria. He was cared for at home, and after many months he was able to walk with a cane. The facial paralysis had cleared, but the left hand remained almost useless. After the stroke his headache disappeared. There was little change in his condition during the next few years. In 1945 and 1946 he had a few generalized seizures, after each of which he had difficulty in articulating for several hours. At no time prior to the stroke had he complained of sudden loss of vision or periodic numbness of the hand.

He was first examined in this clinic in June 1946, three years after onset of the hemiplegia. Neurological examination showed spastic left hemiparesis, the hand being particularly disabled. Nystagmus was present on deviation of the eyes in all directions. Sensation was normal. There was an extensor plantar response on the left. The mental state was difficult to describe, but the patient was intensely hypochondriacal. He complained of pain in the right calf, and arterial pulsations at the ankle were absent bilaterally. The blood pressure was 142/95. The Wassermann reaction of the blood was negative. An electrocardiogram was normal.

In July 1948 gangrene of one of the toes of the left foot appeared. Pulsations were absent in both lower extremities, except in the right femoral artery. No calcification was present in the tibial vessels. In September 1948 a lumbar sympathetic block was followed by a severe reaction of excitation and confusion. There was little change in the patient's condition during the following year except for the development of gangrene of the other toes of the left foot.

On Jan. 24, 1950, in order to test the action of vasodilator drugs on the circulation of the legs, he was given a safe dose of an autonomic-blocking agent. The blood pressure dropped to an unobtainable level, and the patient became ashen gray, confused and apprehensive. Epinephrine was administered, and the patient seemed to recover. A few hours later he became agitated, twisting about in bed with his arms outstretched. He was aphasic and sweated profusely but was not in shock. He constantly attempted to get out of bed and would touch anything near his left hand. Periodically the breathing became Cheyne-Stokes in character. The eyes were deviated to the left, and there was minimal weakness of the left side of the face. From time to time he had transient convulsive movements of all limbs. There was a Babinski response bilaterally. He reacted to painful stimuli. At times he coughed or yawned. The cerebrospinal fluid was within normal limits.

Three days later the patient was in deep coma. No pulsation was felt in the right carotid artery and only a slight one in the left. Pulmonary edema developed, and the patient died five days after the onset of his final illness. Postmortem examination was permitted.

Anatomic Diagnoses.—Necropsy revealed atherosclerosis and old thrombosis of the right internal carotid artery; thrombosis of the right common carotid artery; recent thrombosis of the left internal carotid artery; an area of old encephalomalacia in the right frontal region; a recent one in the left frontal region; pulmonary edema with bronchopneumonia; severe coronary atherosclerosis, and obliterative atherosclerosis of the common iliac arteries.

Neuropathological Studies.—Both cerebral hemispheres showed extensive lesions. The right hemisphere presented an extensive area of old cystic degeneration, involving the outer half of the putamen, the claustrum, the external capsule, the anterior limb of the internal capsule and the inferior frontal gyrus. On the left side, there was recent softening in the territory of the middle and anterior cerebral arteries, but the insula and basal nuclei seemed intact. The territory of the posterior cerebral artery was spared bilaterally. The cerebral vessels were only mildly atherosclerotic. The pattern of the circle of Willis could not be reconstructed.

The right carotid system only was removed. The carotid sinus was completely occluded by dense white tissue. The occlusive process extended into and along the common carotid artery to its origin from the innominate artery. The common carotid artery was a solid cord, about one-half its normal size. Microscopic section showed only dense fibrous tissue, probably the result of organization of a thrombus. The left carotid system was not examined in the neck. Within the skull it was found to be distended with a dark red clot, which extended into the

middle cerebral artery. The picture was so similar to that in case 3 that it was concluded that the final process was the same in both cases, a profound fall in blood pressure allowing thrombosis to take place in the internal carotid artery distal to an atherosclerotic narrowing.

Summary.—This patient had an old hemiplegia, due to thrombosis within the right internal carotid artery. Retrograde thrombosis and consequent organization had extended proximally, to the innominate artery. The cause of the final stroke is regarded as thrombosis of the left internal carotid artery due to vascular collapse, but no confirmation was possible. The clinical history is remarkable in that the patient had had severe recurrent headaches prior to onset of the first attack of hemiplegia.

CASE 5.—A man aged 62 was hospitalized for treatment of chronic contact dermatitis. On Oct. 30, 1949, on awakening from a nap after lunch, he found he could not speak properly. When examined 20 minutes later, he was unable to speak but could carry out commands. There was right hemiparesis, involving the face, arm and leg. Sensation to pinprick was decreased over the entire right side. The tendon reflexes were equal on the two sides, but a Babinski sign was elicited on the right. Breathing was a little rapider than normal. The heart showed normal sinus rhythm, and the blood pressure was 170/90. The patient was slightly confused and was incontinent of urine. The cerebrospinal fluid was under normal pressure, and the findings in other tests were not remarkable.

From the family it was learned that, beginning 10 months previously, he had had many brief attacks of numbness of the right hand, coming on at no particular time and lasting one to two minutes. The patient stated that the sensation was not one of the hand's being "just asleep." In addition, on two occasions he had said, "I just got such a scare; I couldn't talk." These episodes lasted two or three minutes. In one of them, which occurred while there were visitors, he excused himself and went to tend the furnace. Speech returned by the time he came back. There was never a disturbance of vision.

Further investigation revealed absence of pulsation in the left internal carotid artery. The peripheral pulsations in the lower extremities were normal. The Wassermann reaction of the blood was negative. Roentgenograms of the neck revealed a tiny fleck of radiodensity at the bifurcation of the left common carotid artery. Roentgenograms of the skull were not remarkable. A pneumoencephalographic examination was not done. An arteriogram taken on March 29, 1950 showed the passage of the dye to be blocked in the internal carotid artery, just distal to its origin. The external carotid artery filled well. An electrocardiogram was within normal limits.

Summary.—This patient had repeated transient episodes of numbness of the right hand and two transient attacks of aphasia. A final massive right hemiplegia with aphasia came on during sleep. Pulsation in the left internal carotid artery was absent. An arteriogram showed blockage in the left internal carotid artery just above the bifurcation of the left common carotid. A fleck of radiodensity was found in the region of the sinus.

CASE 6.—A man aged 60, having previously been in robust health, awakened on June 17, 1950 with weakness and numbness of the left hand and forearm, associated with frontal headache. His complaints disappeared in a few hours, and he was well until noon of the following day, when the numbness returned in the same region, but again cleared within a few hours. The following morning he awakened with complete paralysis of the left side of the face and the left arm and leg but with little or no change in consciousness. Later, it was ascertained that during the month prior to his admission he had on several occasions lost vision in the right eye for approximately a minute. On one occasion he said to a friend, "I have gone blind in one eye." His friend replied, "Don't worry; it will be all right in a minute," and it was. The patient therefore did not pay more attention to this symptom. For at least two years he had had recurrent headaches on the right side, chiefly above and to the side of the eye, which were steady in nature and lasted from one-half hour to an entire day. The headaches came about once each month and were not severe. He also had other symptoms, which may not have been relevant. For at least one year he had been subject to severe aching deep in the right ear on

going out into the cold air or when, in driving, a stream of air struck his ear. Putting cotton in the auditory canal prevented the pain. He did not have dizziness or deafness. Periodically, for several months, he had had bouts of a peculiar aching pain over the left side of the trunk from shoulder to hip. This feeling passed off in a few hours, and no cause was ever found for it.

The patient was admitted 24 hours after the onset of his stroke. There was total left hemiplegia with sensory deficit and homonymous hemianopsia. He was drowsy, irritable and incontinent. Pulsation in the right internal carotid artery was absent. The blood pressure was 170/90. There was no cardiomegaly, and normal sinus rhythm was present. The cerebrospinal fluid was not examined. Roentgenograms of the skull showed a condition within normal limits. An electrocardiogram was not remarkable. Surgical exposure of the right carotid vessels for arteriography revealed good pulsation in the common and external carotid arteries but none in the internal carotid artery, and no blood could be withdrawn from it.

Recovery has been very slow, the left hand remaining completely useless.

Summary.—This case is remarkable for the premonitory attacks of unilateral blindness and headache. The massive hemplegia was typical. Pulsation of the affected internal carotid artery was strikingly absent.

CASE 7.—A man aged 66 had been well in the past except for a few attacks of sciatica. As a boy he had had "migraine" if he missed a meal.

On Feb. 27, 1950 he arose at 5:45 a. m. One-half hour later, while putting on his shoes, his right hand became paralyzed, and the medial side of the hand and forearm felt as though he had "bumped his funny bone." He was alone and did not have occasion to speak. Fifteen minutes after the onset of weakness the hand was stronger, and he was able to use it in taking tram tickets from his pocket. At 6:40 a. m. he spoke to the tram conductor. In a few minutes his hand became weak again, and, attempting to speak to a friend, he was unable to say a word. Ten minutes later he could speak normally, but the hand remained weak. Aphasia returned for 20 minutes or so at 9 o'clock, and at 10 o'clock it returned and persisted until his admission to the hospital, a few hours later. The leg was not involved, and he did not have dizziness or headache.

For three or four months previously, attacks of blindness of the left eye, lasting from two to four minutes, had occurred repeatedly. The attacks had increased in frequency until they were coming two or three times a week. If he closed his good eye, he was totally blind. In addition, he had had several episodes of numbness of the index finger and the medial half of the middle finger of the right hand and the right forearm. These bouts lasted two to three minutes, and he had had five or six in a period of three or four months. The attacks of blindness never came at the same time as the numbness. At times he lost feeling on the right side of his face, but this was an indefinite symptom. On one occasion he stated that he also had had attacks of numbness around the corner of the mouth on the right side. At no time did he have pounding in the ear, deafness, tinnitus or pain.

As already mentioned, he was admitted shortly after the third, and persistent, attack of aphasia. He could only mumble incoherently but understood speech and the printed word. There was moderate weakness of the right side of the face and the right hand grip. The right leg was strong. Tendon reflexes were increased on the right, and the plantar response was of extensor type. Two point discrimination was impaired over the entire right side of the body. There was no hemianopsia. Pulsation in the left internal carotid artery was absent. Vision was normal in both eyes.

The blood pressure was 180/82. Normal sinus rhythm was present. Arterial pulsations were present in the limbs. An electrocardiogram was normal, except for small Q waves in CF_2. The Wassermann reaction of the blood was negative. Roentgenograms of the skull revealed nothing significant.

By the next day, speech had improved, and the right hand grip was stronger. During the night a short attack of blindness in the left eye had occurred. During the next month strength in the right hand became normal, and the only speech difficulty remaining was a slight tendency to grope for words, associated with mild dysarthria. In the ensuing five months the transient episodes of blindness have continued, occurring as often as once a day. The whole attack lasts about five minutes. For one minute vision becomes progressively "smokier"; then for two

minutes all is black, and recovery takes place over a period of two minutes. In an attempt to find factors related to the onset of these attacks, the patient was asked to keep a diary, but their occurrence seemed to be haphazard, not being related to exercise, sleep, reading, eating or position. Arteriography has been avoided because of the precarious state of the circulation in the left eye.

Summary.—Outstanding in the patient's history were repeated attacks of unilateral blindness, both before and after the major stroke. Prior to the stroke, he had also had transient attacks of numbness. Pulsation in the left internal carotid artery was absent on his admission.

CASE 8.—A man aged 49, at the age of 25, in 1925, while at work, suddenly felt faint and fell to the floor. The left leg below the hip was numb and completely paralyzed. Over a period of two and a half months full recovery occurred, and for 25 years he felt well.

On May 25, 1950, while at work, numbness appeared in the medial two fingers of the left hand and gradually ascended the arm. The hand became weak and useless. Two hours later the left leg became numb and weak. He was able to walk to his home with difficulty. The next morning, on awakening, the left arm and leg were almost useless. Consciousness was not impaired. Three days later he had a severe headache of the type described in the next paragraph. It lasted two hours.

Closer questioning then elicited the fact that for at least seven months he had had attacks of total blindness in the right eye, lasting a minute or so and occurring once each week. For one week prior to admission, he had had a steady headache over the right eye, lasting one or two hours. It was present on arising and made him feel unwell, but it seemed to pass off in the fresh air. It was not throbbing. At least twice in the week prior to his stroke, he had the typical pins and needles sensation in the medial two fingers of the left hand, exactly like the first symptoms of his subsequent stroke. The blindness did not occur after the onset of hemiplegia.

He was first examined several days after the onset of the hemiplegia. There was weakness of the left side of the face and the left arm and leg, the hand having almost no movement. Cortical sensory deficit was present, but there was no hemianopsia. Pulsation was weaker in the right carotid artery than in the left, but that on the left seemed weaker than normal. No bruit could be heard over the carotid vessels. The heart was not enlarged. Normal sinus rhythm was present. The blood pressure was 130/80. The peripheral pulsations were normal in the limbs. Roentgenograms of the skull revealed nothing abnormal. The patient refused permission for an arteriogram.

Summary.—In this case, again, the diagnosis is unverified but it seems warranted on clinical grounds. Premonitory symptoms heralded the final hemiplegia. This is the only case in the series in which another stroke had occurred many years previously.

COMMENT

HISTORICAL REVIEW

For a century and a half, ligation of the carotid vessels has been performed for aneurysm and uncontrollable bleeding, as well as for epilepsy and trigeminal neuralgia. Neurological complications occurred with variable frequency and were not unexpected. Blockage of the carotid artery due to trauma or a gunshot wound, or secondary to local infection, aortic aneurysm or new growth has often been reported. However, recognition that spontaneous occlusion of the carotid vessels takes place as a result of local arterial disease has been long delayed. Chiari,[2] in 1905, found that emboli can break away from thrombus material lying in the carotid sinus and cause apoplexy. He observed thrombus deposited on atherosclerotic plaques in the carotid sinus in seven cases, in a series of 400 consecutive autopsies. The carotid artery was completely blocked in only one case. Hunt,[3] in the United States, examined the carotid pulsation in 20 cases of hemiplegia,

finding it absent on the appropriate side in four instances. He suggested more thorough study of the cervical portion of the carotid artery at autopsy. Full credit for bringing the problem to the attention of clinicians is due to Egaz Moniz, who not only introduced carotid arteriography, but also, in collaboration with Lima and de Lacerda, first described occlusion of the cervical portion of the internal carotid artery.[5] Their report (1937) included clinical details of four cases in which the diagnosis was made by arteriography. The routine use of carotid arteriography has since led to the discovery of many additional cases. Andrell[6] (1943) found 23 cases diagnosed by that means and added nine cases of his own. Moniz (1937) had reported four cases; Löhr[7] (1936), three cases; Shimidzu[8] (1937), one case; Chao and associates[9] (1938), two cases; Riechert[10] (1938), three cases; Siegert[11] (1938), two cases, and Sorgo[12] (1939), eight cases. Hyland[13] had reported a single case in 1933, but pathological examination failed to give full confirmation of the clinical diagnosis. King and Langworthy[14] (1941) described three cases in which the diagnosis was made on clinical grounds, chiefly unilateral optic nerve atrophy combined with contralateral hemiplegia. Galdston and associates[15] described two cases of thrombosis of the carotid vessels in the neck. The paper by Krayenbühl and Weber[16] (1944) contained 16 cases, 11 of them being definite instances of occlusion of the internal carotid artery. Wolfe[17] (1948) presented one case; Taptas and Pecker[18] (1948), five cases (only one definite), and Ameli

5. Moniz, E.; Lima, A., and de Lacerda, R.: Par thrombose de la carotide interne, Presse méd. **45**:977, 1937.

6. Andrell, P. O.: Thrombosis of the Internal Carotid Artery: A Clinical Study of 9 Cases Diagnosed by Arteriography, Acta med. Scandinav. **114**:336, 1943.

7. Löhr, W.: Hirngefässverletzungen in arteriographischer Darstellung: Thrombotische Verstopfungen und Zerreissungen von Gefässen des Gehirns, Zentralbl. f. Chir. **63**:2593, 1936.

8. Shimidzu, K.: Beiträge zur Arteriographie des Gehirns—einfache percutane Methode, Arch. f. klin. Chir. **188**:295, 1937.

9. Chao, W. H.; Kwan, S. T.; Lyman, R. S., and Loucks, H. H.: Thrombosis of the Left Internal Carotid Artery, Arch. Surg. **37**:100 (July) 1938.

10. Riechert, T.: Die Arteriographie der Hirngefässe bei einseitigem Verschluss der Carotis interna, Nervenarzt **11**:290, 1938.

11. Siegert, P.: Die ursächliche Bedeutung einer Verkalkung oder Thrombose der Carotis interna für Funktionsstörungen des Auges, Arch. f. Ophth. **138**:798, 1938.

12. Sorgo, W.: Über den Art. carotis interna—Verschluss bei jüngeren Personen, Ztschr. f. d. ges. Neurol. u. Psychiat. **167**:581, 1939.

13. Hyland, H. H.: Thrombosis of Intracranial Arteries: Report of 3 Cases Involving, Respectively, Anterior Cerebral Basilar and Internal Carotid Arteries, Arch. Neurol. & Psychiat. **30**:342 (Aug.) 1933.

14. King, A. B., and Langworthy, O. R.: Neurologic Symptoms Following Extensive Occlusion of the Common or Internal Carotid Artery, Arch. Neurol. & Psychiat. **46**:835 (Nov.) 1941.

15. Galdston, M.; Govons, S.; Wortis, B. S.; Steele, J. M., and Taylor, H. K.: Thrombosis of the Common, Internal and External Carotid Arteries, Arch. Int. Med. **67**:1162 (June) 1941.

16. Krayenbühl, H., and Weber, G.: Die Thrombose der Arteria carotis interna und ihre Beziehung zur Endangiitis obliterans v. Winiwarter-Buerger, Helvet. med. acta. **11**:289, 1944.

17. Wolfe, H. R. I.: Unexplained Thrombosis of the Internal Carotid Artery, Lancet **2**:567, 1948.

18. Taptas, J. N., and Pecker, J.: Les thromboses de la carotide interne et de ses branches, Rev. neurol. **80**:1, 1948.

and Ashby [19] (1949), six cases. Webster and associates [20] (1950) reported three cases of thrombosis of the common carotid artery and one of thrombosis of the internal carotid artery.

In addition to these clinical reports, Hultquist,[1] in 1942, published his extensive monograph describing the results of the pathological study of the entire carotid system in a series of 1,400 autopsies. He studied the location, pathogenesis, histology and propagation of thromboembolism, giving detailed accounts of the resultant changes in the brain. The monograph, which includes an extensive bibliography, should be consulted by everyone interested in the subject.

Closely related to the condition under discussion are four other syndromes, which will be mentioned only briefly. First is bilateral occlusion of the carotid vessels, represented by a small group of cases. The latest paper, by Frøvig [21] (1946), contains all available references. Second is thromboangiitis obliterans (Buerger's disease) of the cerebral vessels, which has now been reported many times; it is surprising how closely the clinical picture resembles that of occlusion of the internal carotid artery.[22] Undoubtedly, some cases are due to unrecognized disease of the carotid artery, but space does not permit a full discussion of the subject at this point. Third is a syndrome, represented by a large group of cases, in which the clinical picture is that of occlusion of the internal carotid artery but arteriography fails to show complete blockage, there being an irregular narrowing of the vessel at one or several points, in a highly variable fashion. Andrell,[6] Krayenbühl and Weber,[16] Taptas and Pecker [18] and Ameli and Ashby [19] all mention such cases. The last of these related syndromes is spontaneous occlusion of the common carotid artery with a clinical picture, and probably a pathological basis, similar to that of occlusion of the internal carotid artery.

Clinical Aspects

Judging from my cases, the basic feature of spontaneous occlusion of the cervical portion of the internal carotid artery is hemiplegia, often of severe degree, which is usually preceded by premonitory fleeting symptoms, including paresthesias, paralysis, monocular blindness and aphasia. Headache is a common prodromal complaint. These statements do not apply to thrombosis occurring during the severe hypotension of shock, a subject to be discussed later.

Although the basic pattern is fairly constant, the actual clinical picture is a highly variable one, a fact not surprising when it is recalled that the blood supply of an entire cerebral hemisphere, of one eye and perhaps of the brain stem is concerned. Depending on the length of vessel involved and the collateral circulation, as well as the speed and frequency of occlusion, the picture would be expected to include a wide spectrum of neurological symptoms. At one extreme lies the

19. Ameli, N. O., and Ashby, D. W.: Non-Traumatic Thrombosis of the Carotid Artery, Lancet **2**:1078, 1949.

20. Webster, J. E.; Dolgoff, S., and Gurdjian, E. S.: Spontaneous Thrombosis of the Carotid Arteries in the Neck, Arch. Neurol. & Psychiat. **63**:942, (June) 1950.

21. Frøvig, A. G.: Bilateral Obliteration of the Common Carotid Artery: Thromboangiitis Obliterans? Contribution to the Clinical Study of Obliteration of Carotids and to the Elucidation of Cerebral Vascular Circulation, Acta psychiat et neurol. 1946, supp. 39, p. 3.

22. Lindenberg, R., and Spatz, H.: Über die Thromboendarteriitis obliterans der Hirngefässe (cerebrale Form der v. Winiwarter-Buergerschen Krankheit), Virchows Arch. f. path. Anat. **305**:531, 1939.

probability that thrombosis must often take place with few or no symptoms, for surgical ligature of the internal carotid artery can be carried out in many cases without harm. Hultquist found changes in the brain in only one third of cases with occlusion of the internal carotid artery below the origin of the ophthalmic branch. If "silent" occlusion takes place, one must be cautious in attributing bizarre intracranial disturbances to an occlusion as demonstrated by arteriography, for it may be only coincidental.

The cases previously described in the literature have been discovered for the most part during arteriographic studies, in younger patients whose histories led to the suspicion of brain tumor. The present case reports are the result of looking for disease of the internal carotid artery in a group of cases of ordinary "stroke," and it is likely that a representative clinical description will result if materials from the two sources are combined.

The reported age incidence ranges from 7 to the middle 60's, but the great majority of patients have been between 35 and 55 years of age. The relatively large number in their teens or 20's has led to the clinical dictum that unexplained hemiplegia in a young person may well mean thrombosis of the internal carotid artery. The reported age incidence is not strictly representative, however, for seven of the present group were in their 60's. Hultquist, too, found the greatest frequency to be between 50 and 70 for men and between 60 and 80 for women.

All my patients were men, an incidence which is in agreement with the previous report, which showed males to be affected predominantly, in the ratio of 8:1. No doubt, these figures need amendment, but a preponderance in men is probably typical.

Prodromal fleeting attacks of paralysis, numbness, tingling, speechlessness, unilateral blindness or dizziness have been highly characteristic in the present series, all patients but one having experienced them. Case 1 is typical of an uncommon, but spectacular, group. The history was marked by at least 100 attacks of dizziness and speechlessness, associated with numbness and complete paralysis of the right hand. These episodes had occurred over a period of eight months, and between attacks the patient had been well. The other patients usually had but a few transitory attacks before the major stroke, temporary paresthesia of the hand or transient hemiplegia commonly occurring once or twice in the preceding week or month. One patient (case 5) had many brief attacks of numbness of the right hand and at least two attacks of aphasia in the seven months prior to onset of hemiplegia. In case 2 several attacks of "deadness" of the right hand had occurred in the previous month.

Prodromal fleeting symptoms have previously been commented on by several authors, Moniz regarding them as characteristic of his internal carotid artery syndrome. One of his patients had repeated attacks of paresis of the arm and leg over a period of four months. In Andrell's case 3, transient attacks of paresis of the right arm had recurred for several months. Case 8 of Krayenbühl and Weber was marked by one transient attack, in which the patient had the impression he had lost his right hand and his right ski pole, and another in which he was unable to read for one to two hours. The same authors described another patient who on one occasion was unable to read for a moment and on another let a spoon fall for no reason, and a few days later his glasses. The few reported cases of

bilateral occlusion of the carotid system have been characterized by transient attacks of several kinds. The outstanding premonitory symptom in my cases was transient unilateral blindness on the side of the affected artery, and no less than four patients had noted it. In no instance was it a spontaneous complaint, but was simply called "trouble with my eyes" or "blurred vision." Two patients (cases 7 and 8) had had attacks for several months before the hemiplegia, while the others (cases 2 and 6) each had several attacks in the month prior to their stroke. Usually blindness occurred suddenly, "like a blind being lowered," and lasted one-half to two minutes. The blindness in case 7 lasted five minutes, taking two minutes to come on and two minutes to recede, with one minute of complete blindness. Blindness occurred without relation to other fleeting symptoms. Usually it disappeared after onset of the hemiplegia, but in case 7 it was present five months later. Permanent unilateral blindness did not accompany the onset of hemiplegia in any case.

Transient unilateral blindness has been mentioned only once previously in connection with carotid artery disease, one of Andrell's patients (case 7) having had temporary blindness in the left eye, which first appeared two months after the initial stroke. The spells of blindness in that case continued to occur but with gradually diminishing frequency. Moniz described fleeting blindness in 1 case. In Andrell's case 3 there occurred visual disturbances which were thought to be hemianopsic. Reports of fleeting unilateral blindness of undetermined nature, and usually attributed to vasospasm or thromboangiitis obliterans, are not uncommon. Perusal of these reports suggests that often unrecognized carotid disease was responsible.[23] Previous authors have mentioned other visual complaints, such as "glistenings" or "blurred vision," associated with disease of the carotid arteries.

Headache has been so common as to warrant special attention. It occurred in four of the presently reported cases and was situated above the eye on the side of the affected artery. The headache in case 1 was unique in that it accompanied each transient attack of paralysis and aphasia and ceased as the paralysis disappeared. During the headache the temporal vessels on the left side pulsated prominently. In case 4 headache was excruciating and had occurred once a week for a year prior to the onset of the hemiplegia. The headache lasted about half an hour, and the right eye became red and tearful. In case 6 the headache, which was not severe, occurred about once a month and lasted from one-half hour to an entire day. Similar headache was present at the onset of permanent paralysis. In case 8 the patient had had the headache for only one week prior to his stroke. It was present on his arising in the morning, made him feel unwell, lasted from one to two hours and seemed to pass off in the fresh air. A severe bout of the same type of headache occurred three days after he became hemiplegic. In all cases the headache was steady, never throbbing.

The literature on occlusion of the internal carotid artery contains many references to headache, but usually its precise features are not described. Moniz and Andrell both referred to headache, appearing either several years before other manifestations or at a later stage of the disease. Five of Andrell's patients had periodic headaches, all on the same side as the carotid artery involved and situated

23. Foerster, O., and Guttmann, L.: Cerebral Komplikationen bei Thrombangiitis obliterans, Arch. f. Psychiat. **100**:506, 1933.

above the eye, over the temple or at the nape of the neck. Riechert's three patients had headache. It seems common for a bout of headache to precede the onset of hemiplegia by a few hours.

Premonitory mental and emotional changes have been difficult to assess. In some cases, relatives were definite in stating that there had been no change. In others, a "slowing up," lack of energy, irritability and depression have been noticed. The literature is equally indefinite on this point, Andrell simply stating that neurasthenic complaints can herald the onset of symptoms. Emotional depression, even leading to attempted suicide, was reported by Moniz. In Shimidzu's case there was a three year history of depression, insomnia, loss of memory, uncleanliness, dysphasia and logorrhea, the diagnosis before arteriography being Pick's disease.

Dizziness, a frequent complaint in previous reports, was not described in sufficient detail to enable one to ascertain what the patient meant by the term. In case 1 of Moniz, dizziness was associated with headache, seizures and weakness of the right arm. Andrell had a patient with attacks of vertigo so severe she fell down. Riechert,[10] Siegert [11] and Krayenbühl and Weber [16] also mentioned dizziness. In the present series it was noted only in case 1, there being vertigo, rotatory in type, associated with diplopia. However, since the basilar artery was also diseased, the dizziness should not be attributed to occlusion of the carotid artery without further confirmation. Dizziness in case 1 was always part of a constellation of fleeting symptoms.

Several other symptoms have been described, both in my series and in previously reported cases. Attacks of unconsciousness are uncommon, but in case 4 of Krayenbühl and Weber two such attacks preceded by two and one month, respectively, the onset of hemiplegia. One of Andrell's patients (case 6) suddenly fell prostrate, without sequelae. Unconsciousness on exertion has been characteristic of cases of bilateral occlusion of the carotid vessels. Convulsions occurring subsequent to the hemiplegia and arising from damaged cerebral tissue are not unexpected, but focal seizures accompanied attacks of transient paralysis in case 4 of Moniz. In case 8 of Krayenbühl and Weber sudden jerking of the right leg had been noted. Head noises have been remarked on several times. One patient of the present group (case 1) had repeated throbbing in the left mastoid area with each attack of paralysis. One of Moniz' patients had the "tic-tac" of a watch in the left ear for several hours after an attack of aphasia. In Andrell's case 8 there occurred a soft roaring in the head synchronous with the pulse, while another of his patients had a head noise like the roaring of an engine for two months.

Transient diplopia occurred in one of the present cases (case 1) but appears to be infrequent (Moniz, Siegert, Krayenbühl and Weber). One of my patients had painful paresthesias over the trunk and, in addition, had pain in one ear when a stream of air struck it. Two of Andrell's patients had sneezing attacks, one in the earliest stages of the disease and the other only later, when paralysis was persistent.

At the same time that prodromal symptoms are presented in some detail, it must be emphasized that in many reported cases the hemiplegia apparently came out "of the blue."

The arrival of persistent or permanent neurological deficit is extremely variable, but two broad types may be distinguished. The first is characterized by the sudden

onset, within a few minutes or hours, of a massive hemiplegia. It is not infrequent that paralysis is present on awakening from sleep or appears shortly thereafter (in four of my cases). The second is that in which the onset is hesitant or "stuttering," various fractions of a total hemiplegia appearing over a period of days, weeks or months before the picture remains stationary. The present series does not contain good examples of the second type, but one patient (case 6) had two attacks of weakness of the right side 48 and 24 hours, respectively, before the onset of hemiplegia. The signs in case 7 fluctuated for four hours before persisting. The period of onset probably lasted 12 hours in case 8, weakness first appearing in the left arm and following in the left leg two hours later, and by the next morning total paralysis of the left side was present.

The literature is replete with cases of "stuttering" onset, often, however, described too briefly to enable any conclusion as to the nature of the process. One patient of Moniz first had numbness and paralysis of the left hand. Six days later a convulsion of the left side of the face was followed by weakness. A few days later weakness of the left leg occurred, and eight days later sudden complete left hemiplegia appeared. His case 3 was characterized by repeated transient attacks of paresis of the right arm and leg, occurring over a period of four months, aphasia gradually being added. In case 5 of Andrell slurred speech had first occurred for a short time; two days later speech difficulty, somnolence and inability to respond when spoken to appeared, and seven days later there was sudden collapse with left hemiplegia. Another of his patients (case 6) had noted gradually increasing weakness of the right arm, fluctuating for three or four months before mild hemiplegia persisted, while still another patient first had mild right hemiplegia which took a month to clear and then, three months later, a similar attack which did not clear completely. His case 8 was characterized by the gradually progressive development of paralysis of the left side over a period of four months without any recognizable episodic features. Case 9 ran a similar slowly progressive course, without any fluctuation. Two patients of Krayenbühl and Weber had had a progressive, but episodic, course. One first felt the right hand asleep, and a few days later the leg became weak and still later the right arm. The other (case 6) had attacks of speech disturbance and weakness of the right hand, coming with increasing frequency and lasting longer, until the right arm was paralyzed. Case 10 was most unusual, there being a slowly progressive hemiplegia for 13 years. In Wolfe's case there were first weakness of the right arm and aphasia, followed three days later by weakness of the right leg. Most of Ameli and Ashby's patients had a history of weakness of one limb before other regions of the same side were affected. One of their patients first began to drag the right foot; next day the right arm was weak, and one month later a transitory speech defect developed. Case 4 was marked by progressive hemiplegia of three years' duration.

Cases in the literature probably represent a highly selected group, as it is just the patients with a history of progressive hemiplegia who would require an arteriogram to rule out an expanding intracranial lesion. A slowly progressive hemiplegia should be attributed to occlusion of the internal carotid artery only as a last choice.

As stated previously, the neurological picture is highly variable, but there is always hemiplegia of some degree. Patients with a sudden onset of complete paralysis usually have a cortical sensory deficit and homonymous hemianopsia,

with aphasia if the dominant hemisphere is involved. Consciousness may be impaired, aphasia frequently magnifying the degree of unresponsiveness. Drowsiness, urinary incontinence and nocturnal restlessness are common. When the onset is more gradual, the process often stops at the stage of mild or partial hemiplegia, and the prognosis is much more favorable. Field defects and sensory deficit in general vary with the severity of the paralysis.

In the present series the retina was not examined during a period of blindness. Lindenberg and Spatz [22] have given a detailed account of how the retinal vessels gradually became "snow white" and then as redness reappeared vision returned. The authors did not appreciate the probable presence of occlusion of the internal carotid artery. Foerster and Guttmann [23] reported a case in which repeated attacks of blindness occurred in the right eye. One attack occurred under ophthalmoscopic examination, and vision was lost first in the lower field. The vessels running to the upper part of the retina became bloodless. Permanent unilateral blindness and optic nerve atrophy, usually on the basis of occlusion of the central retinal artery, have been reported several times in cases of thrombosis of the internal carotid artery but are by no means typical. Krayenbühl and Weber mentioned the test of Bailliart [24] for determining the pressure in the central retinal artery of each eye. The test assumes that the pressure in the central retinal artery is lower on the side of the occluded internal carotid artery. Papilledema, unilateral or bilateral nystagmus, anisocoria and paralysis of the third or sixth nerve have been mentioned in the literature several times, but are uncommon. Two of the present series of patients had nystagmus. Otherwise, the pupils and the ocular movements were normal. Sorgo found miosis on the side of the thrombosed artery in six of eight cases. Andrell reported paralysis of vertical ocular movement in one case. Galdston and associates [15] found marked sensitivity of the carotid sinus on the side opposite the occluded vessel in two cases, pressure quickly producing seizures and unconsciousness.

Mental change following the hemiplegia is of course invariable, aphasia often adding to the disability. In his patients Moniz noted euphoria and inability to appreciate their illness. Excessive smiling and agreeableness were seen several times in my cases and were attributed to damage to the frontal lobe. On the other hand, patients can be querulous, impatient and depressed. Even in the mildest cases there is usually some failure of highest mental function, often recognizable as inability to maintain attention in difficult situations, a tendency to lower the level of general interest, to choose easier hobbies and to fall into inferior reading habits. The wife of one patient noted no change in her husband, except that he was easier to handle.

The value of palpation for the carotid pulsation in the neck has been much disputed. It appears to me to be of great help, especially a short time after the major stroke. Later, with recanalization, pulsation may return, as in case 2. Palpation must be carried out as high up in the neck as possible, and the characteristic expansile thrust should be identified. Pulsation in the external carotid artery is not confusing if high palpation is done, for the external carotid artery soon divides into many branches of relatively small caliber. Of course, if thrombosis

24. Bailliart, P.: Circulation artérielle rétinienne: essais de détermination de la tension artérielle dans les branches de l'artère centrale de la rétine, Ann. d'ocul. **154**:257, 1917.

has occurred in the intracranial portion of the internal carotid artery, pulsation in the neck will not be affected. This is of great importance, as Hultquist found primary thrombosis in the internal carotid artery in the region of the posterior communicating artery about one third as often as in the region of the sinus. However, the occlusion in the present series was always in the region of the sinus. When thrombosis has extended proximally to block the common carotid artery, pulsation will usually be lost in the superficial temporal vessels, but Galdston and associates reported an exception to this rule, the temporal pulsation being present, although the common carotid artery was completely blocked. A bruit was not heard in any case, although sought for routinely over the carotid vessels.

The cerebrospinal fluid in the acute stage probably reflects the size, type and position of the infarct, by showing a slight rise in the pressure and in the cell and protein contents. The fluid is usually clear, any infarction of brain tissue being of the pale type, but in one case of Ameli and Ashby the fluid was bloody. This is an appropriate place to emphasize that routine lumbar puncture in cases of acute stroke is not only useless but harmful, and is against the soundest dictates of neurological experience and theory. Herniation of uncal or cerebellar tissue, and later death, often result from the withdrawal of lumbar cerebrospinal fluid in the face of acutely rising intracranial pressure due to edema of the brain or cerebral hemorrhage. In view of this danger, data on the changes in the cerebrospinal fluid are meager in the present series.

Roentgenograms of the skull are usually noncontributory. Roentgenologic study of the neck may show a small fleck of calcification in the carotid bulb. A pneumoencephalogram in the late stage will show ventricular enlargement paralleling the size of the cerebral softening. Carotid arteriography is the only means of making the diagnosis during life, short of surgical exploration. Arteriograms usually demonstrate a complete block in the region of the carotid sinus. However, several cases of partial block at the sinus or within the carotid siphon have been described, but, as none of these has been studied pathologically, their interpretation is uncertain. Since the clinical picture in the latter cases is identical with that resulting from total occlusion, it is not unlikely that recanalization has taken place, although there is no good evidence for this conclusion.

General examination of patients with occlusion of the internal carotid artery is of interest. Arterial hypertension has been absent oftener than present; but, again, neurosurgeons may have avoided patients with hypertensive vascular disease when considering arteriography. The presence of high blood pressure may augment the tendency to fleeting symptoms, as in case 1. The theory that thromboangiitis obliterans is the underlying pathological process has led several authors to appraise the vascular system in detail. In none has the classic clinical picture of this condition been present. On the other hand, the frequency with which coronary atherosclerosis, cardiac infarction, angina pectoris, peripheral gangrene, intermittent claudication and absence of pulse at the ankle accompany disease of the internal carotid artery is in keeping with the generally accepted idea that the process is atherosclerotic. However, in young persons, there need not be evidence of generalized atherosclerosis. Of my patients, two had had cardiac infarction; one, occlusion of an iliac artery, and another, peripheral gangrene. An uncommon feature mentioned by Moniz and Andrell is a superficial pigmented nevus, probably a coincidental finding.

The severe hemiplegia resulting from occlusion of the internal carotid artery carries a gloomy prognosis, and extensive disability often persists. However, some patients make very nearly a complete recovery, and especially is this so when the onset has been "stuttering," or gradual. Death in the acute stage is not common, probably a good reason that cases of this stage have not been recognized pathologically. The fact of long survival is evidenced by those young hemiplegic patients who have lived 30 or 40 years without further incident.

Diagnosis

Distinctive Features.—Briefly, the syndrome is characterized by hemiplegia of sudden or gradual onset, usually heralded by few or many attacks of fleeting symptoms, including paresis of a limb, paresthesias, aphasia and monocular blindness. The occurrence of transient unilateral blindness is probably diagnostic in itself, but it is not infrequently absent. Headache is common and typically is situated over the eye on the side of the affected artery. It is periodic and steady rather than throbbing. Often the onset of hemiplegia occurs in steplike fashion over a period of weeks or months, one part after another becoming involved. Males are predominantly affected. Most cases occur between the ages of 50 and 80, but cases of persons as young as 15 have been reported. The hemiplegia may be severe or mild; when severe, it is usually associated with impaired consciousness, sensory deficit, homonymous hemianopsia and incontinence of sphincters. In milder cases the patient is usually spared these. Mental change is to be expected.

The absence of pulsation in the internal carotid artery is important, especially in the acute stage. The only certain methods of making the diagnosis are carotid arteriography and surgical exposure of the carotid vessel. Occlusion of the vessel in most cases is in the carotid sinus, but it may also occur just distal to the ophthalmic branch. The cerebrospinal fluid is usually clear. Roentgenograms of the skull show nothing abnormal. Pneumoencephalograms will only confirm focal loss of cerebral tissue. Since the pathological basis is atherosclerosis, the patient will usually have other evidence of the same process in the coronary, peripheral or cerebral arteries.

Differential Diagnosis.—The most important factor in differentiation is to keep the diagnosis in mind and to remember that occurrence of the condition is not uncommon. Occlusion of any one of several other cerebral arteries can reproduce the clinical picture very closely. It has been pointed out previously that in a large series of cases occlusion of the middle cerebral artery was found to be most uncommon, and fortunately so, for differentiation from disease of the internal carotid artery is virtually impossible unless episodic unilateral blindness occurs. Occlusion of the anterior or posterior cerebral artery may well have associated premonitory symptoms, but persistent widespread motor and sensory signs are uncommon. If the most proximal portion of the posterior cerebral artery is affected, hemiplegia may occur. Thrombosis of the anterior choroidal artery can also produce a picture similar to the one under discussion.

There is not space at present to enter into a detailed differentiation of occlusion of the internal carotid artery from cerebral embolism, cerebral hemorrhage, leaking aneurysm, bleeding into a tumor and other conditions liable to produce hemiplegia. Since I regard lumbar puncture as contraindicated, especially in cases of cerebral hemorrhage, differentiation is usually made on the basis of a detailed history and a complete general, as well as neurological, examination.

It is not likely that the syndrome will be confused with epilepsy, although in a few cases unconsciousness and focal seizures have preceded paralysis. The diagnosis of migraine is often made in these patients, for the headache is indeed of that type. It can only be suspected that migraine starting late in life might be due to disease of the internal carotid artery. Until a method is found to circumvent the occurrence of a major stroke in these patients, the differentiation is largely an academic one. That the headache should so closely mimic migraine is, however, of more than passing interest.

Pathology

This part of the discussion refers only to "spontaneous" occlusion of the carotid artery, and not to thrombosis following ligature or disease of the surrounding structures. The literature is especially lacking in pathological data pertaining to occlusion of the internal carotid artery. Necropsies in which the brain and cervical portions of the carotid arteries have been investigated are rare. The brain alone has been examined only a few times. Most information has been obtained indirectly and by the study of pieces of artery resected at operation. Good clinicopathological correlation awaits further postmortem study.

The structures showing pathologic alterations can be conveniently divided into three parts: (1) the carotid arteries, (2) the brain and (3) the circle of Willis.

Carotid Arteries.—In spite of the fact that in the past the cervical portion of the internal carotid artery has apparently been examined completely only once or twice at autopsy, there is fairly good agreement that atherosclerotic change in the region of the carotid sinus is the pathological basis of thrombosis of the internal carotid artery. Sorgo, Riechert, Andrell, and Webster and his associates have all found atherosclerosis in a resected portion of the involved artery. Krayenbühl and Weber, also examining surgically resected specimens, found atherosclerosis alone in three cases and combined with thromboangiitis obliterans in three cases. Hultquist, in his routine postmortem studies, showed clearly that atherosclerosis was the fundamental change.

It has been known for many years that the first portion of the internal carotid artery is especially liable to atherosclerosis. Mehnert [25] found the intensity of the atherosclerotic change there to be second only to that in the abdominal aorta. Chiari, after examining the carotid vessels in 400 cases, concluded that the internal carotid artery was affected just as severely as the abdominal aorta. He found atherosclerosis of the carotid sinus in two boys aged 12 and 18 and in two women aged 23 and 25, with very little atherosclerosis elsewhere. In recent years, the discovery of the physiological importance of the carotid sinus had led to further studies in this area. Keele [26] examined 55 consecutive unselected cases, studying the condition of the arch of the aorta and the bifurcations of the innominate, carotid and common iliac arteries. He found changes in the carotid sinus area in 50 cases. Atherosclerosis was present in a patient as young as 16, but was severer in the older age group. The degree of change in the internal carotid artery paralleled that seen in the iliac arteries. Hasselbach [27] also examined the vessels in 72 cases,

25. Mehnert, cited by Chiari.[2]

26. Keele, C. A.: Pathological Changes in the Carotid Sinus and Their Relation to Hypertension, Quart. J. Med. **2**:213, 1933.

27. Hasselbach, H.: Bestehen Beziehungen zwischen Veränderungen am Sinus caroticus und der Hypertonie? Beitr. z. path. Anat. u. z. allg. Path. **86**:369, 1931.

in only three of which changes were absent. Therefore the evidence is strong that atherosclerosis is the fundamental pathological change underlying thrombosis of the internal carotid artery.

However, Andrell, Antoni,[28] Krayenbühl and Weber and others have not infrequently observed the pathological picture of thromboangiitis obliterans. Almost all their opinions are based on the histological study of resected portions of the artery, and the descriptions they give seem not to justify the diagnosis. Mural inflammatory cells and delicate fibrillar connective tissue within the lumen have been the two most important criteria for the diagnosis of thromboangiitis obliterans. But focal collections of chronic inflammatory cells occur frequently within atherosclerotic plaques, and fibrillar connective tissue may be the late result of the organization of a thrombus. Thromboangiitis obliterans of the smaller cerebral arteries, rather than the major trunks, has been described by Antoni, Lindenberg and Spatz and others. However, in all three of Antoni's cases there was also occlusion of the internal carotid artery, which was held to be incidental. The other authors also state that thrombosis of the internal carotid artery was present in a number of their cases. It is important that in suspected cases of cerebral thromboangiitis obliterans the carotid systems be carefully examined. In short, further proof is necessary before thromboangiitis obliterans of the carotid and cerebral arteries can be accepted.

The involved vessel was examined at autopsy in four of the cases in this series. The region of the carotid sinus was selectively involved by atherosclerosis in all cases. The lumen of the artery was either entirely occluded or narrowed to a diameter of 0.5 or 1.0 mm. Recanalization had probably followed thrombosis in case 2. As a rule, the carotid bulb was firm to palpation and cut with "grating." The lumen when present was situated eccentrically. The occlusion was conical, so that the narrowest portion of the lumen might be localized to a length of the vessel no greater than 1 to 2 mm. This is mentioned to indicate how hazardous it might be to base a conclusion on a resected portion of vessel. The atherosclerotic mass extended from the sinus down at least to the angle of bifurcation of the common carotid artery, and in case 4 it lay partly in the terminal portion of this vessel. In case 4, also, organized thrombus extended down the common carotid artery to its origin from the innominate artery, reducing the vessel to a firm cord. Thrombosis of the common carotid artery has been reported on several occasions [15] and is no doubt often due to thrombosis in the region of the bifurcation, with secondary retrograde thrombosis. The internal carotid artery above the sinus was normal in each case. The common carotid artery, except, of course, the one which was thrombosed, showed slight atherosclerosis. Although in all cases in the present group occlusion of the carotid artery was present in the region of the sinus, Hultquist, as previously mentioned, found that occlusion in the intracranial portion of the internal carotid artery in the region of the posterior communicating artery was one third as frequent, a significant number, to be sure.

The histological appearance of the region of the occlusion was the same in all cases. The adventitia and media were not altered. The lumen was filled with abundant subintimal connective tissue, in which lay atheromatous material, choles-

28. Antoni, N.: Buerger's Disease, Thrombo-Angiitis Obliterans in the Brain: Report of 3 (4) Cases, Acta. med. Scandinav. **108**:502, 1941.

terol crystals and foam cells. Special stains for fat showed heavy deposits throughout this tissue. Microscopic thrombus material was attached to the wall in one case. There was no diffuse inflammation, but nests of round cells lay scattered at the junction of the atheroma and the media. Small endothelium-lined channels were abundant within the subintimal mass and represented either recanalization or the vessels of chronic granulation tissue.

A striking feature was the occurrence of occluding atheroma in the carotid sinus of one side, while the opposite sinus showed almost no atherosclerosis. Also, the severity of change in the carotid sinus was not reflected in the intracranial vessels. In cases 2, 3 and 4 there was very little cerebral atherosclerosis, and had the carotid vessels not been examined, one would have been at a loss to explain the large lesion of the brain.

In case 3, in which thrombosis occurred during postoperative shock, a large fresh clot distended the internal carotid artery above the atherosclerotic plaque and extended into the middle and anterior cerebral arteries. In case 4 there was also a recent clot in the internal carotid artery, but the cervical portion of the vessel was not examined. In that case, too, thrombosis occurred during hypotensive shock.

In case 1, in addition to an extremely narrowed left internal carotid artery, the basilar artery had considerable narrowing, with recent secondary thrombosis. The relative importance of the basilar and carotid occlusions is not clear, but this case illustrates the necessity for complete examination at autopsy in achieving a reliable clinicopathological correlation.

Brain.—The large area of destruction of the brain in cases 2 and 4 on the right side is probably typical of the chronic phase of severe hemiplegia due to thrombosis of the internal carotid artery. A cystic atrophic lesion replaced the outer portion of the lenticular nucleus, the anterior limb of the internal capsule, the head of the caudate nucleus, the insula and most of the frontal lobe. Hultquist found approximately the same area affected and concluded that the lesions usually occur in the anterior portion of the area of distribution of the middle cerebral artery. Antoni examined the brain of one of Andrell's patients and noted softening of the parietal lobe. In Sorgo's case there were extensive lesions of the two hemispheres. It is impossible to generalize from so few cases, and no doubt there will prove to be many variations in the extent of involvement of the brain, especially of the frontal lobe, as the collateral circulation through the anterior communicating artery is highly variable. In case 2 the temporal lobe was entirely spared, but not in case 4. In case 2 at least two more areas of softening lay posterior to the main lesion. The explanation for these variations is not known, but anastomotic vessels connecting the anterior, middle and posterior cerebral arteries on the surface of the hemisphere are possibly responsible. An unexpected finding in case 1 was a softening in the territory of the left calcarine artery; and, as the posterior communicating vessels were small, the softening was felt to be due to basilar thrombosis or embolism. Otherwise, in case 1 there were no gross lesions, although the patient had had repeated transient attacks of paralysis and aphasia for eight months.

In case 3, in which extensive postoperative thrombosis had occurred, there was a large area of swollen, soft brain in the territory of the middle and anterior cerebral arteries. The picture was typical of that seen after acute occlusion of a cerebral artery from any cause.

Circle of Willis.—The circle of Willis has not been described in previous reports. It could be reconstructed in three of my autopsy cases. In case 1, the anterior cerebral artery was large, the left posterior communicating artery, of medium size and the right posterior communicating artery small. Collateral blood could therefore pass easily from one side to the other, but not from the basilar to the carotid artery or the reverse. The hemodynamics in this case are not clear, but it is possible that the internal carotid arteries, especially the right one, supplied considerable blood to the basilar territory for many months. Finally, occlusion of the basilar artery took place, and the collateral carotid supply, alone, was no longer adequate. In case 2, the posterior communicating arteries were small, and the anterior communicating artery was large. Yet the frontal lobe was greatly affected, which should not occur if the anterior communicating artery were adequate. Section of this artery showed that it was evidently not a single vessel but consisted of at least four smaller vessels within its lumen, and where they were attached to the right anterior cerebral artery the walls of the constituent vessels were so thickened as to occupy most of the lumen. Thus, what appeared at first to be a large adequate artery proved on section to be inadequate. In case 3 the posterior communicating arteries were small, and two tiny, threadlike vessels represented the anterior communicating artery. Infarction of the territory of the anterior and middle cerebral arteries is therefore clearly explained.

In summarizing the pathological data, it can be said that (1) the occlusion of the internal carotid artery is usually in the region of the sinus; (2) the pathological basis is atherosclerosis; (3) changes in the brain tend to be localized in the territory of the middle and anterior cerebral arteries, and (4) the extent of the brain lesion is explained partly by the anatomic pattern of the circle of Willis, but partly by additional, unknown, factors.

Mechanism Underlying Production of Symptoms

Severity of the Neurological Deficit.—It has just been mentioned in the conclusions of the preceding section that the extent of damage to the brain following spontaneous occlusion of the internal carotid arteries is a function of the adequacy of the collateral circulation. It is usually possible to explain most of the pathological picture by closely studying the vascular pattern and the patency of its vessels. But the pattern of the circle of Willis must be studied in its entirety. For example, it is not sufficient to examine the anterior communicating artery and, finding it large, conclude that failure of collateral circulation cannot be used to explain the pathological picture. The size of the involved anterior cerebral artery must be considered too, for it may be small and inadequate when the anterior communicating artery is ample (fig. 9*C*). A large posterior communicating artery may be a liability, rather than an asset, if the proximal posterior cerebral artery is small. If the anterior communicating and posterior communicating arteries are small, the territory of the middle and anterior cerebral arteries will be infarcted. If the anterior communicating artery is small and the posterior communicating artery is large, the entire hemisphere will usually be softened. Figure 9 shows a few of these relations.

Transient Attacks.—The fundamental disturbance underlying the fleeting attacks of blindness, aphasia, paresis and paresthesia is, of course, unknown. These symptoms have been attributed in the past to cerebral "vasospasm," a phenomenon

which has so far defied attempts at elucidation. The temporary symptoms usually last one-half to five minutes but may continue for 30 minutes or an hour. Episodes of unilateral blindness in no case coincided with attacks of aphasia or paresthesia. If it is assumed that vascoconstriction is responsible for the symptoms, this could mean that the vascular change is limited to one segment of the carotid tree at any one time. This would also mean that temporary constriction of the internal carotid artery in the region of the atherosclerotic narrowing was not responsible for symptoms, for then blindness and aphasia, for example, would be expected to occur simultaneously. Patients who have been having attacks of unilateral blindness do not become permanently blind in the affected eye at the time of the final hemiplegia.

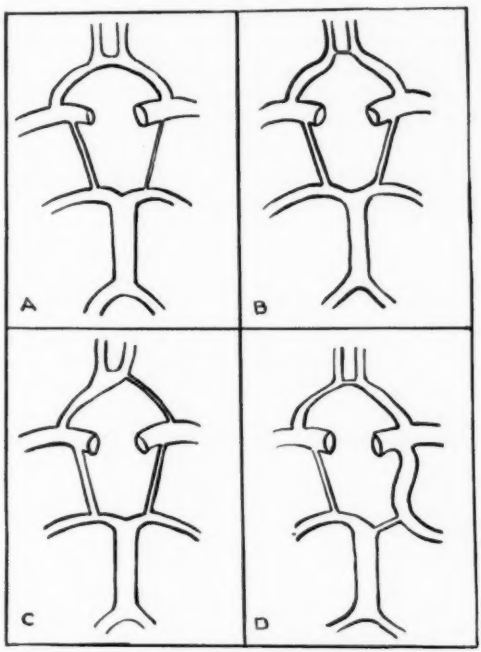

Fig. 9.—Diagram of the commoner forms of the circle of Willis (see text).

If thrombosis and complete occlusion of the internal carotid artery occur at the time of the major stroke and blindness on that side does not occur, it is reasonable to conclude that temporary occlusion of the internal carotid artery has not been responsible for the previous attacks of temporary blindness. The problem is not that simple, however, for attacks of temporary blindness usually cease after the onset of the hemiplegia, indicating that the narrowed portion of the internal carotid artery plays a part. It is significant, too, that attacks occur only a relatively short time before total occlusion of the internal carotid artery and become more frequent as that event is approached. The development of a heavy throbbing in the mastoid area in case 1 suggests a distinct vascular change locally, probably in the internal carotid artery.

"Vasospasm," or, better, vasoconstriction, may temporarily occlude a lumen already extremely narrowed by atherosclerosis. The remaining lumen usually lies eccentrically, bordering on a relatively normal portion of vessel wall, whose smooth muscle tone could influence the size of the remaining channel. On the few occasions that the fundi were examined during transient blindness, a snow white retina was seen, indicating that total interruption of blood flow does occur. That vasoconstriction can produce total ischemia, albeit temporary, in the territory of supply of cerebral arteries would be a most important principle to establish. So far, it is impossible to say whether vasoconstriction of a relatively healthy branch is responsible or whether further narrowing in the vicinity of the atherosclerotic plaque is responsible. The significance of such knowledge in the elucidation of the pathogenesis of migrainous aura need not be stressed. The fact that a clinical picture identical with that of occlusion of the internal carotid artery can occur when the arteriogram shows a channel still existing led Andrell to postulate that the final hemiplegia might well be due to temporary vasoconstriction, rather than to thrombosis. This view can by no means be dismissed lightly, for in three of the present cases a channel still persisted in the region of the carotid sinus.

Hultquist and Andrell stated the belief that impulses arising in the region of the abnormal carotid sinus produced vasoconstriction and changes in the cerebral blood flow in the territory of the carotid artery, even on the opposite side. This would not be a unique property of the carotid sinus, for transient attacks are also part of disease of the basilar and posterior cerebral arteries. The role of sympathetic impulses, normal or abnormal, in producing vasoconstriction can only be surmised, but it is not unlikely that they play an important part. The effect of sympathetic block during the period of intermittent symptoms should be tested. A survey of the influence of hypertension on the frequency of attacks would be interesting, for the fluctuation in vascular tone in high blood pressure should produce more frequent attacks of fleeting symptoms. In case 1, the only one in which significant hypertension was present, there were many more attacks than in the others. However, multiple attacks do occur in normotensive persons.

The phenomena attending immediately on ligation of the carotid artery might be expected to throw light on the transient attacks. Dorrance[29] wrote:

> . . . At the moment of ligation or immediately thereafter, the patient may experience a sense of fainting combined with nausea and vomiting, cold sweat, ringing in the ears and darkening of the fields of vision. These symptoms may be of a few seconds' duration only.

This statement suggests that careful attention to these symptoms would be helpful in understanding the pathogenesis of transient attacks. The delayed onset of symptoms following ligation of the carotid artery is well known but poorly understood. This delay, if not due to thrombosis or emoblism, indicates that in spontaneous occlusion of the internal carotid artery there may be a wide discrepancy between the time of vasoconstriction and the onset of transient symptoms.

Another possible explanation of fleeting symptoms is that the final thrombus rebuilds itself several times before finally holding. This would be tenable in cases in which symptoms occur only a few days before the final stroke but not in those in which transient attacks dated back six or seven months.

29. Dorrance, G. M.: Ligation of the Great Vessels of the Neck, Ann. Surg. **99**:721, 1934.

Changes in the general circulation have often been used to explain transient attacks, but they seem to play no part except that occasionally transient symptoms occur on waking from a sleep, but this is rare. However, often a major stroke is precipitated during sleep, the fall in circulatory rate no doubt being responsible. Whether the hemiplegia follows thrombosis or is directly due to ischemia is of importance, for in the case of the latter an arteriogram would not necessarily show total obstruction. However, in two of my cases in which paralysis occurred during sleep there was total obstruction in the carotid sinus. Fleeting symptoms on exertion occur in cases of bilateral occlusion of the internal carotid artery, probably due to a temporary decrease in cerebral circulation.

Headache.—Little is known of the pathogenesis of the migraine-like headache so frequently seen in the present cases. In fact, it is not widely recognized that intermittent headache is associated with disease of the internal carotid artery. The headache is steady and is situated above the ipsilateral eye and perhaps on the temple. It is episodic, is of moderate severity and is likely to occur in the morning. Headache may occur for years before the final stroke, and it is not unusual for severe headache of the same type to recur at the time of the stroke. Headache as a rule does not come at the time of the fleeting symptoms, indicating that the mechanisms are different. If the fleeting symptoms are due to vasoconstriction, one is tempted to attribute the headache to vasodilatation, a theory which is well in keeping with that of the pathogenesis of headache in general.[30] Pain over the eye is not usually considered to accompany cervical lesions, and in this regard the concept will have to be broadened. Headache usually ceases after the onset of hemiplegia, suggesting that the disorder is in the internal, not the external, carotid artery. That the occurrence of headache for several years before the stroke is just a coincidence is possible, but one patient at the onset of his stroke was able to say, "There is that pain in my eye again." He had been having "that pain" periodically for many years. In some cases of migraine in which hemiplegia has occurred, carotid occlusion may well have been present. In case 1 headache accompanied the episodes of dizziness, aphasia and paralysis and at that time the temporal vessels throbbed prominently. In case 4 the eye was reddened at the time of the headache. Whether the pain is referred from the carotid sinus or is due to local vascular dilatation might be settled if procaine infiltrated at the sinus quickly abolished the headache.

Further speculation is not warranted now, but the recognition of this additional cause of headache may help to elucidate the problem in general.

EMBOLISM FROM THE CAROTID SINUS

Chiari studied this problem in great detail. His interest was stimulated by a case of cerebral embolism in which no source of embolic material could be found. He finally opened the carotid vessels in their entire length and in one carotid sinus found thrombus material deposited on an atherosclerotic ulcer. The depression in the thrombus from which the embolic plug had separated could be identified. Chiari then examined 400 cases and observed gross parietal thrombosis in the region of the carotid bifurcation in seven cases. In four of these cases cerebral embolism

30. Wolff, H. G.: Headache and Other Head Pain, ed. 1, New York, Oxford University Press, 1948.

had occurred, the source of the embolism being the carotid sinus. I have so far been unable to corroborate Chiari's observations in detail but have not infrequently noted thrombus material on the wall of the carotid sinus. Emboli can thus be expected to complicate the picture of internal carotid artery disease, and in case 8 of the present series the sudden monoplegic episode at the age of 25 might well have been due to an embolus. The rare cases in which hemiplegia has occurred during massage of the carotid sinus may be also explained in this way. Further work is needed to assess the importance of Chiari's views, and it is for this reason that brief attention is drawn to it at this time.

APOPLEXY FOLLOWING OPERATION OR VASCULAR COLLAPSE

In recent years several cases of this condition have been studied personally at autopsy, and a long red antemortem thrombus could be withdrawn from the intracranial portion of the internal carotid artery. Since the cervical portion of the carotid artery was not examined, the real cause of the clot was not appreciated. Case 3 is representative of the small, but important, group of cases of postoperative stroke. Hemiplegia following operation is a serious complication and often ends fatally. The history is of an unusual fall in the blood pressure during the surgical procedure, of failure to respond properly thereafter and of gradual appreciation by the attending staff that hemiplegia is present. Severe edema of the brain occurs; a tentorial herniation results, and death usually follows. The pathological picture in case 3 was fairly typical, although thrombosis occurred on the same side as the operation, thus raising the possibility that the thrombosis was due not so much to the vascular collapse as to surgical manipulation. The internal carotid artery was narrowed by atherosclerosis to a diameter of 1.0 mm., and clotting had taken place distally, but not proximally. In case 4 an autonomic-blocking agent was given to test the vascular response in the lower limbs. Vascular collapse occurred, after which the patient lapsed into unconsciousness and presented a complicated neurological picture. Although only one internal carotid artery was examined in the neck, it is felt, in view of the great similarity pathologically to case 3, that the other internal carotid artery was seriously narrowed at its origin. The fall in blood pressure resulted in thrombosis of the only functioning internal carotid artery, producing the picture of decerebration. A year previously lumbar sympathetic block was performed, and the patient had become excited, restless, confused and anxious.

Although the clinicopathological correlation in these two cases is not as clearcut as could be desired, the general conclusion can be made that in cases of hemiplegia following operation or vascular collapse the internal carotid artery in the neck must be examined. The full explanation for hemiplegia occurring during the vascular collapse of myocardial infarction, gastrointestinal hemorrhage or transfusion reaction will be found only if the entire carotid system is explored.

TREATMENT

On this subject there is little definite to state. Following Leriche's theory [31] that impulses arising at the site of local vascular disease cause peripheral vasoconstriction, several authors (Andrell, Krayenbühl and Weber and others) have

31. Leriche, R.: Das Problem der Arteritis obliterans, Med. Welt **9**:851, 1935.

carried out resection of the diseased portion of the internal carotid artery and ligature of the common and external carotid arteries. No striking benefit has resulted. It is claimed that periarterial sympathectomy or cervical sympathectomy has been of benefit in cases of cerebral endarteritis obliterans.[23] I have had no experience with these procedures. However, this raises the important question of the value of cervical sympathetic block in cerebrovascular disease in general. The reports so far are not conclusive, and further studies are needed. Sympathetic block might well prove beneficial in the prehemiplegic phase of internal carotid artery disease, and it is even conceivable that some day vascular surgery will find a way to by-pass the occluded portion of the artery during the period of ominous fleeting symptoms. Anastomosis of the external carotid artery, or one of its branches, with the internal carotid artery above the area of narrowing should be feasible. Prolonged use of anticoagulants (heparin and bishydroxycoumarin U. S. P. [dicumarol®]) is at present being tried when the patient is seen at the stage of intermittent symptoms, but favorable conclusions will have to be made cautiously because of the great uncertainty in the natural progress of the disease. It is hoped that with the use of anticoagulants reendothelization will take place before the occurrence of the final disastrous occlusion.

SUMMARY

Eight cases of occlusion of the internal carotid artery are presented. The pathological data in four cases are included. The characteristic clinical and pathological pictures are outlined. The mechanism of the production of symptoms is discussed briefly.

CONCLUSIONS

Occlusion of the internal carotid artery is much commoner than has heretofore been believed. The carotid sinus is the region of predilection. The basic pathological process is atherosclerosis.

The clinical picture is highly characteristic, although variable. The basic feature is hemiplegia of rather severe degree, preceded by premonitory paralysis, paresthesia, blindness, dizziness, aphasia or unconsciousness. Headache is very common.

Fleeting neurological symptoms, previously attributed to vasospasm, now have a pathological substratum which will serve for their further study.

A new type of headache is described. It is characteristic in location and nature. Its mechanism is unknown.

The exact diagnosis of occlusion of the internal carotid artery rests on arteriography or pathological study, but the clinical features should serve to distinguish it in most cases. Hemiplegia of unknown cause in persons in the younger age group is often due to disease of the internal carotid artery.

The absence of carotid pulsation in the neck during the acute phase of hemiplegia may be diagnostic.

Postoperative hemiplegia, as well as stroke following vascular collapse, is often due to thrombosis of the internal carotid artery distal to extreme atherosclerotic narrowing in the region of the carotid sinus.

Unexplained cerebral embolism may arise from thrombotic material lying in the carotid sinus.

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INTRAMEDULLARY TUMORS OF SPINAL CORD AND GLIOMAS OF INTRADURAL PORTION OF FILUM TERMINALE

Fate of Patients Who Have These Tumors

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ONE OF the observations that impressed us while we were engaged in a study of pathologically verified intramedullary tumors of the spinal cord [1] was the long duration, 4.8 years, of the preoperative symptoms of these tumors, as compared with the corresponding periods, 2.5 and 2.9 years, respectively, for the extradural and the intradural but extramedullary tumors. In view of the small size of the spinal cord and the compactness of its functioning constituents, this temporal difference was unexpected. Eighteen years had passed since this study was reported; and if we were not to lose altogether the opportunity to glean whatever additional knowledge this group of patients may offer, it behooved us to learn what became of them.

It was obvious that a larger number of patients would offer certain advantages, and since the main purposes of this study would still be served, the series was augmented to include all patients having pathologically verified intramedullary tumors of the spinal cord above the conus and filum terminale who had been seen at the Mayo Clinic from 1916 through 1939. Of these there were 74. Also included in this survey was a previously reported group of 25 cases of gliomas of the intradural portion of the cauda equina or filum terminale [2]; additional cases have been added to these to make a total of 45 cases of glioma in this location. This study, then, is based on 119 cases of intramedullary tumors of the cord proper plus gliomas of the conus and filum terminale. Included also are 5 cases of extramedullary gliomas; the total is 124 cases.

It was interesting to note that of our entire series of intraspinal neoplasms 22.5 per cent were intramedullary gliomas, and of this group it was of further interest to note that half were in the lumbosacral segments (charts 1 and 2).

Read at the Seventy-Fifth Annual Session of the American Medical Association, Section on Nervous and Mental Diseases, San Francisco, June 26 to 30, 1950.

1. Kernohan, J. W.; Woltman, H. W., and Adson, A. W.: Intramedullary Tumors of the Spinal Cord: A Review of 51 Cases, with an Attempt at Histologic Classification, Arch. Neurol. & Psychiat. **25**:679-699 (April) 1931.

2. Kernohan, J. W.; Woltman, H. W., and Adson, A. W.: Gliomas Arising from the Region of the Cauda Equina: Clinical, Surgical and Histologic Considerations, Arch. Neurol. & Psychiat. **29**:287-305 (Feb.) 1933.

Unavoidable difficulties are encountered in making a study of this type, and the reader must be invited to make due allowances for errors which our poor judgment may have introduced. Even at the time of an original examination, it was sometimes difficult to decide whether or not an antecedent and isolated attack of lumbago represented the earliest symptom of a tumor. This is especially true when pain

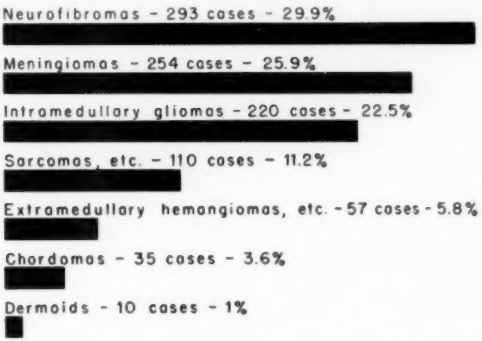

Chart 1.—Classification of 979 intraspinal neoplasms.

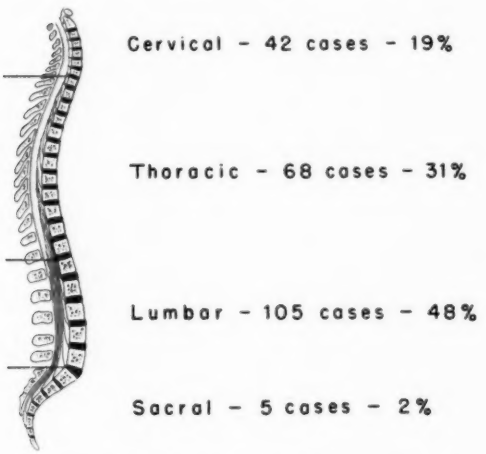

Chart 2.—Distribution of 220 classified intramedullary gliomas.

follows an injury or accompanies pregnancy. On the other hand, when one of our patients related that five years before examination she had become temporarily, but completely, paralyzed below the neck after a fall on ice, this was taken to represent the earliest symptom of a hemangioendothelioma, which was found later to be situated high in the cervical portion of the cord. Likewise, everyone has experienced the difficulty that may be encountered in deciding whether or not a tumor has recurred.

A just criticism is that only a few of these patients were examined by us personally during the past year. Most of the information was obtained by writing to both the patient and the referring physician. Letters addressed to patients were simple and short. They solicited answers to the following questions: Can you work? Can you walk? Can you feel in your legs? Can you control the acts of your bowel and bladder? The patient was requested to encircle the appropriate answer, "Yes" or "No." Considering the long interval of time that had elapsed since most of these patients had been seen, the number of responses (81 per cent) was encouraging.

REPORT OF ILLUSTRATIVE CASE

Since one of these replies was particularly informative as to the vagaries of intramedullary tumors, a brief résumé of the case serves well as a background against which the whole subject we are attempting to portray may be viewed.

CASE 1.—A teamster, aged 41, registered at the clinic Dec. 9, 1925, because of backache, paralysis and incontinence. Two years previously a heavy object he was helping to lift was dropped. He "saw stars" and thereafter had much pain in the thoracic portion of the back and collapsed whenever he jumped. Within a year he had lost completely all power and sensation below the level of the fourth rib and control of his bowels and bladder.

On Dec. 18, 1925, Dr. Adson removed in part an intramedullary ependymoma, grade 1, myxopapillary type. Roentgen treatment was given. This was followed by some return of sensation; he became able to walk with crutches, and he regained partial control of sphincters. On Nov. 17, 1929, four years later, he wrote, "I dug 20 bushels of potatoes; I do the chores and besides take care of my sick wife." He reported that his right leg was a little weak.

On Jan. 4, 1949, Dr. H. H. Hepburn, of Edmonton, Alba., Canada, supplied the rest of the story. "For the first three years following his operation he was unable to walk without support but got around on crutches or with canes. He then became able to drive a motor car, although his legs were spastic. He had fair control of the bowel but not much of the bladder. He was obliged to wear a urinal when away from the house. In 1938, he fell and sustained a fracture of one tibia and fibula, which healed normally without delay. In 1944, he was doing light work, when he fell and sustained a bruise on his right hip; an ulcer developed, which never healed. He was in the hospital two or three times during the next eighteen months with attacks of cellulitis and phlebitis surrounding this ulcer, which finally became very large with necrosis of the great trochanter. On his last admission, he was in the hospital from August 1945 until he died on Dec. 2, 1945 [twenty years after operation]. The immediate cause of death was secondary infection in his chronic ulcer, which resulted in septicemia.

"After death I removed the spinal cord. I may say that he had been bedfast for three months before he died. On removal, the spinal cord showed considerable narrowing and sclerosis from the seventh cervical to the third dorsal segments. At the third dorsal segment there was a slight enlargement of the cord which was surrounded by a mass of scar tissue. This was at the lower limit of the laminectomy. On sectioning this scar tissue, unmistakable foci of the original tumor were found. There was one about 0.5 cm. in diameter and two or three smaller ones completely surrounded by dense scar tissue. He had had several courses of deep x-ray therapy during the first five years after the operation. In the largest mass of tumor cells there was a small central cavity surrounded by cuboidal tumor cells. Dr. Macgregor, our pathologist, classified this tumor as myxopapillary ependymoma. . . . He had had no x-ray therapy for at least five years before he died and there had been no increase in his paraplegic signs during the last 10 years of his life."

METHOD OF PRESENTATION OF DATA

In the interest of brevity, but primarily for the purpose of ready inspection, the data relevant to our survey have been arranged in diagrammatic and tabular forms. The manner in which the cases have been grouped and treated is evident from the legends; diagrams and tables supplement each other, and the corresponding cases appear in the same grouping and order. It was not our

purpose to include a detailed analysis of the symptoms or findings, but it may be said that nothing that is not already common knowledge was encountered. Our comments concern the ependymomas and astrocytomas particularly, since these constitute the larger groups.

EPENDYMOMAS

Of 61 ependymomas, 26 were intramedullary tumors situated above the conus, 14 involved the conus and filum terminale and 21 involved the intradural portion of the filum only (table 1). Hereafter the first group will be referred to merely as intramedullary ependymomas.

All Groups

Sex.—Of the intramedullary group, 17 occurred in men and 9 in women; of the conus and filum terminale group, 8 occurred in men and 6 in women; of the filum group, 14 occurred in men and 7 in women. Taken together, 39 ependymomas occurred in men and 22 in women.

This rather consistently maintained ratio suggests that ependymomas occur more commonly in males. As will be seen later, the difference in sex incidence was not so apparent in the group of astrocytomas.

Age.—The ages of the patients who had ependymomas at the time of operation were as follows: The average age of men who had intramedullary ependymomas was 40.7; the median age was 43. The average age of the women was 38; the median age was 39. The average age of men who had ependymomas of the conus and filum terminale was 31, and the median age, 30; the average and median ages of the women were 28 and 25, respectively. The average age of men who had ependymomas of the filum terminale was 34, and the median age 33; the average and median ages of the women were 31.7 and 33 years, respectively.

Although the incidence of ependymomas in this series was greater in men than in women, men were affected later than women. Men were also affected later by astrocytomas.

The average age of patients who had ependymomas of the conus and filum terminale was about 3 years less than was that of patients who had tumors of the filum only and 10 years less than that of patients who had intramedullary tumors of the cord proper. The reason for this was not apparent.

Intramedullary Group (Situated Above Conus)

Duration and Survival Period.—The duration of the disease was of special interest to us. The preoperative duration of symptoms in the cases of intramedullary ependymoma averaged five years; the median for the group was four years, the longest duration being 17 years and the shortest eight months; the survival period after operation averaged 7.2 years, with a median of five years, the longest period being 27 years (tumor removed and patient still living). The total duration, including the duration of symptoms before operation in cases in which the tumors could be removed and in which the patients were still living, averaged 12.2 years, with a median of nine years, the longest period being 36 years. This patient is still alive and in relatively good health. The shortest duration of the disease from onset of symptoms to death was two years and two months; the operation of splitting the cord presumably did not alter the course of the disease (chart 3 and table 1).

TABLE 1.—*Intramedullary Ependymomas of Spinal Cord Exclusive of Filum Terminale and Conus: Twenty-Six Cases* *

Case	Age; Sex	Symptoms	Level	Operative Procedure	Roentgen Therapy	Duration, Yr.			L or D †	Comment
						Preoperative	Postoperative	Total		
					Grade 1					
1 ‡	41 M	Pain; numbness	Th 1-5	Subtotal removal	+	2	20	22	D	Farming; condition stationary 10 years; patient died of decubitus ulcer
2	40 M	Weakness; numbness	C 4-6	Removal	..	4	12	16	L	Fireman
3 ‡	52 F	Pain; incontinence	Th 4-6	Cord split	..	2	22	24	D	Paraplegia
4 ‡	34 M	Pain; incontinence	Th 11-L 1	Removal	..	9	27	36	L	Working; slight difficulty in walking
5	52 M	Impotence; numbness	Th 1-4	Removal	..	10	0.1	10.1	D	.....
6	31 M	Numbness; weakness	Th 4-6	Biopsy	+	1.5	8.3	9.8	D	Paraplegia; recurrence; ulcers; death from hemorrhage from popliteal artery
7 ‡	22 F	Pain; incontinence	Th 8-10	Subtotal removal	..	0.8	8.6	9.4	D	Paraplegia
8 ‡	46 M	Numbness; pain	Th 8-10	Biopsy	..	9	11 da.	9	D	With syringomyelia
9	57 F	Numbness	C 2-7	Subtotal removal	..	7	0.5	7.5	D	.....
10 ‡	37 M	Pain; weakness	Th 1-4	Biopsy	..	1	6.6	7.6	D	Recurrence
11 ‡	48 M	Numbness; weakness	Th 1-?	Cord split	..	0.7	4.3	5	D	Weaker after operation
12 ‡	26 M	Weakness; incontinence	Th 10-?	Cord split	+	1	1.6	2.6	D	.....
13 ‡	46 M	Pain; weakness	Th 4-10	Cord split	..	2	0.1	2.1	D	Postoperative paraplegia
14 ‡	43 M	Numbness; weakness	Th 8-12	Removal	..	5	16	21	?	Cobbler; paraparesis
15 ‡	43 F	Pain	Th 9-L 3	Decompression	+ and radium	12	5	17	L	Bloody cerebrospinal fluid; cerebellar exploration negative; bilateral choked disks; paralysis of sixth nerve
16	41 F	Numbness; weakness	Th 3-6	Biopsy	..	2	14	16	?	.....
17 ‡	21 F	Pain; numbness	Th 2+	Biopsy	..	7	5	12	D	.....
18 ‡	57 M	Spastic numbness	Th	Decompression	+ and radium	5	2	7	?	.....
19 ‡	51 M	Numbness; weakness	Th 9	Decompression	..	7	5	12	D	.....
20	50 F	Pain; incontinence	Th 2-3	Subtotal removal	..	1.1	2.5	3.6	D	Postoperative paraparesis
					Grade 2					
21	53 M	Numbness; pain	Th 8-9	Removal	..	17	8	25	D	Recurrence; "cerebral hemorrhage"
22	55 M	Numbness; pain	C 4-7	Removal	..	10	2 days	10	D	.....
23 ‡	35 M	Incontinence; weakness	Th 3	Cord split	..	6	2	8	D	Paraplegia before operation
24	41 M	Pain; weakness	C 3-Th 1	Subtotal removal	+	2	3	5	D	Working some
25 ‡	36 F	Pain; numbness	C 1-7	Decompression	+	4.5	0.1	4.6	D	Sister had intramedullary tumor of cord C 2-Th 6
					Grade 3					
26	37 F	Pain; weakness	C 5-6	Subtotal removal	+	1.5	11.5	13	L	Still some pain

Abbreviations used in tables in this paper:

* Patients seen from 1916 through 1939; follow-up to Jan. 1, 1949.

† L means living; D, dead.

‡ Case included among those reported by Kernohan, Woltmann and Adson in 1931 and 1933. Diagnosis was made in 1929 or earlier.

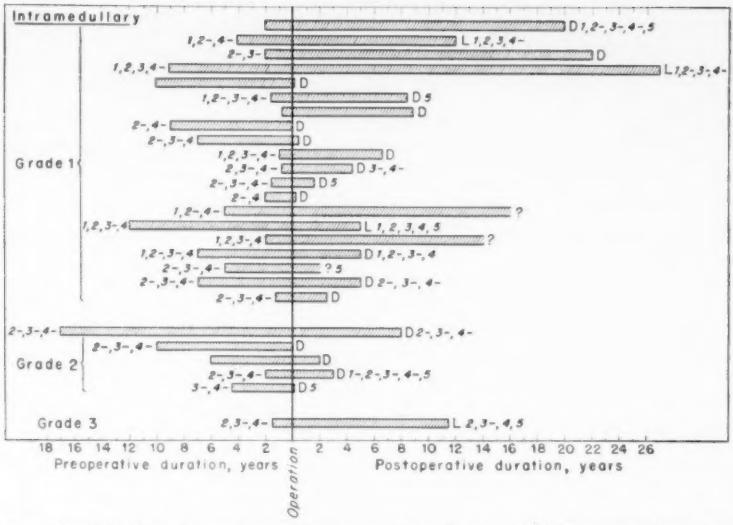

Chart 3.—Duration of symptoms before operation and of survival after operation: data in cases of ependymona of the spinal cord, exclusive of the conus and filum terminale (cases 1 to 26; table 1). Key to abbreviations in this chart and in charts 4 to 7: *D* means dead; *L*, living; *1* that the patient can work; *2*, that he can walk; *3*, that he can feel in the legs; *4*, that he can control acts of the bowel and bladder; *5*, that he has had roentgen therapy. A minus sign (—) after the numeral denotes that the function indicated by the number is impaired. Numerals to the left of the line indicating operation signify the condition before operation; numerals to the right of this line, the condition at time of follow-up examination.

All patients (cases 1 to 124) were seen prior to 1940; follow-up studies were made up to Jan. 1, 1949.

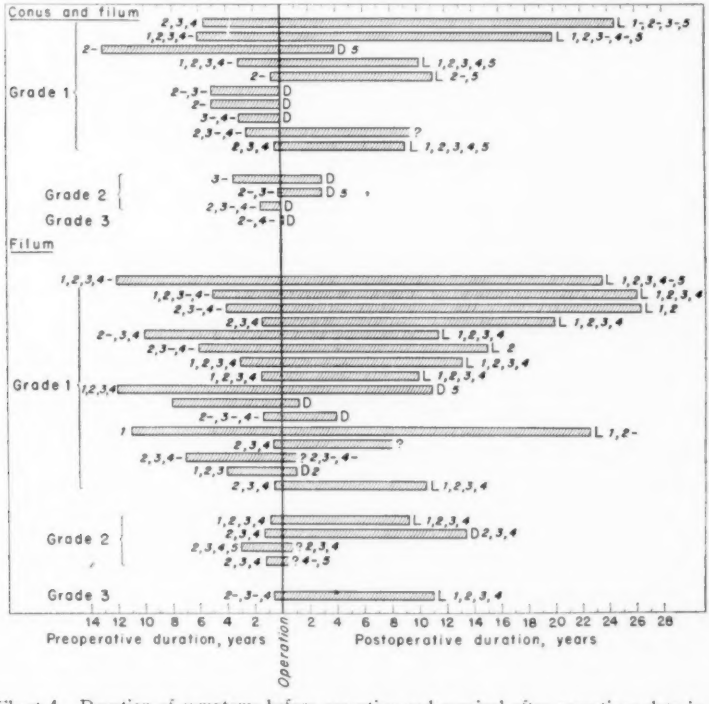

Chart 4.—Duration of symptoms before operation and survival after operation: data in cases of ependymoma of the conus and filum terminale (cases 27 to 61 inclusive; tables 2 and 3).

Symptoms.—Of the 26 patients who had intramedullary tumors, 15 complained of pain, and the same number had experienced numbness; 12 complained of weakness and 6 of sphincteric disturbances.

Operation.—At operation, tissue was removed for biopsy only in five cases; the tumor was decompressed also in nine; a subtotal removal was done in six, and the tumor was removed in six.

Conus and Filum Terminale

Duration.—The duration of the disease of the 14 patients having ependymomas that involved the conus and the filum terminale may be resolved into the following

Table 2.—*Ependymomas of Conus and Filum Terminale: Fourteen Cases* *

Conus and Filum						Duration, Yr.				
Case	Age; Sex	Symptoms	Level	Operative Procedure	Roentgen Therapy	Preoperative	Postoperative	Total	L or D †	Comment
					Grade 1					
27 ‡	33 M	Pain	Th 10-L 5	Removal	+	5.5	24.2	29.7	L	Recurrence; ulcer
28 ‡	29 M	Pain; weakness	Conus	Subtotal removal	+	6	20	26	L	.....
29 ‡	49 F	Pain; incontinence	Conus	Subtotal removal	+	13	4	17	D	Recurrence; carcinoma of cervix
30	21 F	Pain	Conus	Removal	+	3	10.1	13.1	L	Well; two children since
31	19 M	Pain; numbness	Conus	Biopsy	+	0.7	11.1	11.8	L	Incontinence; ulcer; walks with great difficulty
32 ‡	26 M	Pain; incontinence	Caudal	Biopsy	..	5	4 days	5	D	Meningitis
33	23 F	Pain; numbness	Th 11-L 2	Subtotal removal	..	5	9 days	5	D	.....
34 ‡	28 F	Pain; weakness	Caudal	Subtotal removal	..	3	0	3	D	.....
35 ‡	32 M	Pain	L 3-4	Removal	..	2.5	9.5	12	?	Conus resected
36	27 F	Pain	Th 12-L 2	Removal	+	0.2	9	9.2	L	Working well
					Grade 2					
37 ‡	21 F	Pain; weakness	Caudal	Subtotal removal	..	3.5	3	6.5	D	Recurrence
38 ‡	14 M	Pain; weakness	Caudal	Biopsy	+	0.1	3	3.1	D	.....
39 ‡	39 M	Retention; weakness	Caudal	Biopsy	..	1.1	3 days	1.1	D	Acute meningitis
					Grade 3					
40	56 M	Numbness; weakness	Caudal	Biopsy	..	18 days	1 mo.	1.5 mo.	D	.....

periods: The duration of symptoms before operation averaged 3.5 years, with a median of three years, the longest being 13 years and the shortest 18 days; the duration of symptoms after operation averaged 6.1 years, with a median of three years, the longest duration being 24 years; the total duration, including postoperative survival for patients who were those still living, averaged 9.6 years, with a median of 5.5 years, the longest duration being 29.7 years and the shortest 1½ months (chart 4 and table 2).

Thus it appears that patients who had ependymomas of the conus and filum fared less well than did those with intramedullary ependymomas above the conus.

It will be recalled, also, that the patients who had tumors of the conus and filum were the youngest of those in the three groups.

Symptoms.—Of these 14 patients, 12 had complained of pain, 6 of weakness, 3 of numbness and 3 of incontinence.

Intradural Portion of Filum Terminale Only

There remain for consideration 21 cases of ependymoma of the filum only.

Duration and Postoperative Survival.—The duration of symptoms before operation averaged 4.5 years, with a median of three years, the longest duration of symptoms before operation being 12 years and the shortest about six months. The

Table 3.—*Ependymomas of Filum Terminale: Twenty-One Cases* *

Case	Age; Sex	Symptoms	Level	Operative Procedure	Roentgen Therapy	Duration, Yr. Preoperative	Duration, Yr. Postoperative	Duration, Yr. Total	L or D †	Comment
					Grade 1					
41 ‡	32 M	Pain; incontinence	L 4-S 3	Subtotal removal	+	12	23.5	35.5	L	Well; incontinent
42 ‡	35 M	Pain; incontinence	Filum	Removal	..	5	26	31	L	Banker; rancher
43 ‡	23 M	Pain; numbness	Filum	Scooped out	..	4	26.1	30.1	L	Farmer; incontinent
44 ‡	35 F	Pain	L 3-5	Removal	..	1.4	20	21.4	L	.....
45	33 F	Pain	L 2-3	Removal	..	10 (?)	11.3	21.3	L	Like a million dollars
46	37 M	Pain; incontinence	L 4-S 3	Removal	..	6	15	21	L	Walks; no work; incontinent
47	31 F	Pain	L 2-3	Removal	..	3	13.2	16.2	L	Well
48	33 M	Pain	L 1	Removal	..	1.5	10	11.5	L	Neurosis
49 ‡	41 M	Pain	Filum	Subtotal removal	+	12	11	23	D	Recurrence (?) decubitus ulcer
50 ‡	39 F	Pain; weakness	L 1-S	Subtotal removal	..	8 (?)	1.1	9.1	D	Paraplegia before operation
51	26 F	Pain; weakness	Th 9-L 2	Subtotal removal	..	1.3	4	5.3	D	Recurred; decubitus ulcer
52 ‡	26 M	Pain	L 2-S 2	Removal	..	11	22.5	33.5	?	Works; walks; incontinent
53	41 M	Pain	Filum	Removal	..	0.6 (?)	8	8.6	?	Lumbago before operation
54 ‡	33 F	Incontinence; pain	Filum	Removal	..	7	1	8	?	.....
55 ‡	29 M	Pain	Th 12-L 5	Removal	..	4	1	5	?	.....
56	50 M	Pain	Filum	Removal	..	0.6 (?)	10.5	11	L	Well
					Grade 2					
57	19 M	Pain	Filum	Subtotal removal	..	0.7	9.3	10	L	Well
58 ‡	22 M	Pain	S	Removal	..	1.2	13.3	14.5	D	Pulmonary tuberculosis
59	33 M	Pain	L 3-4	Removal	+ before operation	3	0.6	3.6	?	.....
60 ‡	57 M	Pain	L 4-S 4	Subtotal removal	+	1.3	0.3	1.6	?	.....
					Grade 3					
61	25 F	Pain; weakness	Filum	Removal	..	1 (?)	11	12	L	"Fine"; housework

duration of survival after operation averaged 10.7 years, with a median of 11 years, the longest being 26.1 years, and this patient is still living. The total duration of the disease, including postoperative survival periods of the patients still living, was 15.2 years, with a median of 13 years, the longest being 35.5 years, and the patient is still living.

The long survival period of some of these patients may seem irrelevant except for one noteworthy point, i. e., that in a number of cases the tumor, like porridge, had to be "scooped out." This can only mean incomplete removal. This occurred in the case of the patient who is still living (and farming), 26.1 years after operation,

and of the patient who has the longest history, 35.5 years, and is still living and, it may be added, working (table 3).

Thus, it will be seen that patients who had ependymomas involving the conus and filum terminale fared worst. Those with intramedullary tumors at a higher level fared better, and those with tumors of the filum only fared best.

Symptoms.—Of the 21 patients, all had had pain, and 20 mentioned it as the first symptom and several as the only symptom. Four complained of incontinence, 3 of weakness and 1 of numbness.

Thus, the early appearance of symptoms other than pain should suggest, in the case of low-lying tumors, that the conus is probably involved.

Cases Which Teach Certain Lessons

Before leaving the ependymomas, a number of cases ought to be referred to briefly, since they were especially instructive.

A problem in diagnosis and procedure was presented by a woman (case 15, table 1), aged 43, who for 12 years before coming to the clinic had had rectal pain, the onset of which followed an operation for uterine prolapse. One month before coming to the clinic she had experienced in the occiput a succession of 12 attacks of intense pain; these had lasted three or four minutes only. After one of these attacks she was left with diplopia. The spinal fluid was found to be bloody.

Examination at the clinic revealed choking of the optic disks, of 4 D., weakness of the external rectus muscles of the eyes, nystagmus, slight delay in recognition of pinprick in the perianal region, pale yellow cerebrospinal fluid obtained on cisternal puncture and bright yellow fluid and evidence of subarachnoid block on lumbar puncture. Exploration of the posterior fossa disclosed no surgical lesion. Eighteen days later an intramedullary ependymoma, situated between the ninth thoracic and the third lumbar vertebra, was decompressed and the region irradiated. The patient last was heard from five years after operation, at which time she reported that she was restored to health.

Another case of an intramedullary ependymoma must be mentioned for whatever it may signify. This concerned a woman (case 25, table 1) whose tumor extended from the first to the seventh cervical vertebra and who had a sister, as we learned from Dr. Paul Bucy, in whom he found an intramedullary ependymoma extending from the second cervical to the sixth thoracic segment.

One would be pleased, but not necessarily surprised, to have the report from a patient 12 years after an intramedullary ependymoma had been removed from the fourth to the sixth cervical vertebra, that he is a fireman, but one would not anticipate that a patient (case 4), aged 52 at the time her spinal cord was split for an inoperable ependymoma, would be alive 22 years after operation.

ASTROCYTOMAS

Considering briefly the astrocytomas, we shall confine our comments, for purposes of comparison with the intramedullary ependymomas, to the intramedullary astrocytomas, of which there were also 26 cases. The conus and filum groups were too small to permit of separate analysis (table 4).

Intramedullary Group (Situated Above Conus)

Sex.—Ependymomas occurred oftener in men than in women. Astrocytomas, however, occurred about equally in men and women, the incidence being 14 and 12, respectively.

TABLE 4.—*Intramedullary and Extramedullary Astrocytomas of Spinal Cord Exclusive of Filum Terminale and Conus: Thirty-One Cases* *

Case	Age; Sex	Symptoms	Level	Operative Procedure	Roentgen Therapy	Duration, Yr.			L or D †	Comment
						Preoperative	Postoperative	Total		
				Intramedullary Astrocytomas, Grade 1						
62 ‡	21 F	Pain; paralysis	C 6-Th 3	Biopsy	..	7	31.5	38.5	L	Sews; paralyzed; "excellent health"
63	36 M	Pain; numbness	Th 1-5	Decompression	+	3	9.5	12.5	L	Paraplegia
64 ‡	27 F	Pain; numbness	C 1-7	Subtotal removal	+	4.3	6	10.3	D	Recurrence
65 ‡	58 M	Pain; numbness	Th 11-12	Cord split	+ and radium	6	0.2	6.2	D	.....
66 ‡	62 M	Pain; weakness	Th 9-12	Subtotal removal	..	3.5	0.4	3.9	D	Decubitus ulcer
67	24 F	Pain; weakness	Th 6-8	Biopsy	+	1.5	1.3	2.8	D	.....
68 ‡	40 F	Pain; weakness	Th 2	Removal	..	13	2	15	?	Paraplegia
69	43 F	Ataxia; pain	Th 4	Biopsy	..	4	17	21	D	Also had multiple sclerosis
70	22 M	Weakness; incontinence	Conus	Biopsy	..	0.1	8	8.1	?	Walks; incontinent; fathered a child
71	43 M	Spasticity	Th 2-4	Biopsy	..	4	1.6	5.6	?	Tumor with cyst
72 ‡	50 M	Pain; numbness	C 5-Th 2	Cord split	..	2.5	0.1	2.6	?	.....
73 ‡	61 M	Numbness; weakness	Th 11-L 2	Biopsy	..	1	0.1	1.1	?	.....
				Intramedullary Astrocytomas, Grade 2						
74	45 F	Pain; weakness	C 3-6	Subtotal removal	+	8	18.2	26.2	L	Works; mild combined sclerosis; neurosis
75	39 M	Pain; weakness	Th 5-10	Biopsy	+	5	16.1	21.1	L	Works; walks; "I get along"
76	9 F	Weakness; pain	C 3-Th 4	Biopsy	+	7.5	13.1	20.6	L	Paraplegia; cheerful
77	52 M	Pain; numbness	C 1-Th 1	Biopsy	..	10	11.3	21.3	D	Recurrence; cardiac death
78	48 M	Pain; weakness	Th 8	Subtotal removal	..	0.6	2.5	3.1	D	Recurrence
79	17 M	Weakness; numbness	C 6-8	Decompression	..	0.1	2	2.1	D	Paraplegia; recurrence
80 ‡	21 F	Pain; numbness	C 6-7	Biopsy	..	1	3 wk.	1	D	.....
81 ‡	52 F	Weakness; numbness	Th 2-3	Cord split	..	9	0.4	9.4	?	Paralysis; incontinence
82	39 M	Pain	Th 12	Biopsy	+	4	1.6	5.6	?	Deaf; choked disk; carcinoma of lung (?)
				Intramedullary Astrocytomas, Grade 3						
83	28 F	Pain	Th 10-L 2	Removal	+	3	13	16	L	Getting on well
84	32 M	Pain; weakness	Th 12	Biopsy	+	1.2	4.8	6	D	Recurrence
85	61 F	Pain; numbness	Th 2-4	Decompression	..	0.6	1.5	2.1	?	Recurrence
86 ‡	32 F	Numbness; weakness	Th 8-12	Decompression	..	1	0.6	1.6	D	Paraplegia
87 ‡	25 M	Pain; weakness	C 1-5	Decompression	..	0.2	5 days	0.2	D	Choked disks; meningeal metastasis
				Extramedullary Astrocytomas, Grade 1						
88	20 F	Pain; weakness	C 8-Th 2	Removal	..	3.7	0	3.7	D	Paraplegia before operation
89	28 M	Pain; weakness	Th 10	Removal	+	0.5	0.6	1.1	D	Paraplegia
90 ‡	42 F	Pain; numbness	L 1-2	Removal	..	0.5	0.1	0.6	D	Uremia
				Extramedullary Astrocytomas, Grade 2						
91 ‡	30 M	Mass	Lumbar	Removal	+	15	15	30	?	Extradural, hard mass
92 ‡	59 M	Pain; weakness	Th 12-L 3	Removal	..	2	16	18	D	Works; walks; stroke

Age.—The average age for men at time of operation was 41.8 years, and the median age, 41; the average age of the women was 33.6, and the median age, 30.

Here, as with ependymomas, women were affected earlier in life than men.

Duration and Survival.—The duration of symptoms before operation averaged 3.9 years, with a median of three years, the longest duration being 13 years and the shortest one month. The period of survival after operation averaged 5.9 years, with a median of two years, the longest period being 31.5 years. The total duration, from the appearance of the first symptoms, including the postoperative survival periods of patients still living, averaged 9.8 years, with a median of six years; in

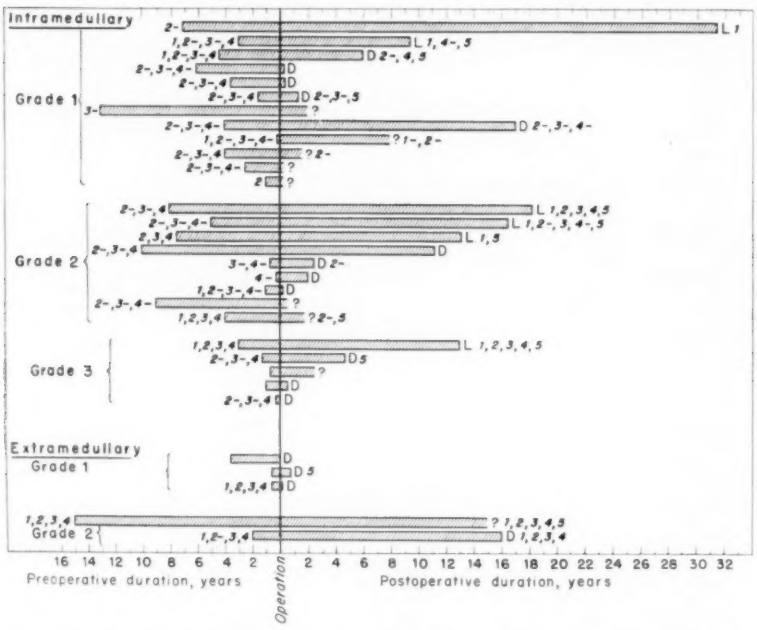

Chart 5.—Duration of symptoms before operation and survival after operation: data in cases of astrocytomas of the spinal cord, exclusive of the conus and filum terminale (cases 62 to 92 inclusive; table 4).

this average is included the period of survival to Jan. 1, 1949, of those still living. The longest duration was 38.5 years; the patient who had survived for this period reported that he was in "excellent health." The sohrtest total duration was three months (chart 5 and table 4).

These figures suggest that patients who have intramedullary astrocytomas do not fare as well, by about two years, as do patients who have ependymomas.

Symptoms.—Of these 26 patients, 20 had complained of pain, 14 of weakness, 10 of numbness and 1 of ataxia.

Operation.—At operation tissue was removed for biopsy only in 12 patients; the tumor was decompressed also in 8; subtotal resection of the tumor was accomplished in 4, and the tumor was removed in 2. This suggests that the possibility of removing an astrocytoma is less than that of removing an ependymoma.

Extramedullary Group (Situated Above Conus)

There were five extramedullary astrocytomas; four of these were within the dura, and one was extraspinal and in the lumbar subcutaneous tissue (chart 5 and table 4).

Table 5.—*Miscellaneous Tumors of Conus and Filum Terminale: 10 Cases* *

Case	Grade	Age; Sex	Symptoms	Level	Operative Procedure	Roentgen Therapy	Duration, Yr. Preoperative	Duration, Yr. Postoperative	Duration, Yr. Total	L or D †	Comment
					Astrocytoma of Conus and Filum						
93	1	48 M	Incontinence; weakness	Th 12-L 5	Removal	..	2	11	13	L	Incontinence; "well"; works
94 ‡	2	20 F	Weakness; pain	Th 11	Subtotal removal	+	1	1.7	2.7	D	Paraplegia
					Astrocytoma of Filum Only						
95 ‡	1	27 F	Pain; weakness	Th 11-L 4	Removal	..	4	30	34	D	No recurrence; dementia; Pick's disease (?)
96 ‡	1	52 M	Pain	L 2	Removal	..	10	22	32	D	Cardiac death
97 ‡	1	61 F	Cramps; incontinence	L 1-2	Removal	..	15	7 days	15	D	Meningitis; pes cavus
98	1	47 M	Pain	L 3-S 1	Subtotal removal	+	2 (?)	10	12	D	No recurrence; cause of death (?)
99 ‡	1	34 M	Pain (horse kick)	L 1	Removal	..	2.2	3 wk.	2.2	D	Meningitis
					Oligodendroglioma of Filum Only						
100	1	28 F	Pain	L 2	Removal	..	3	2.2	5.2	D	Worked; well; death from "bowel obstruction"
101 ‡	2	36 F	Pain; numbness	Filum	Removal	..	1	4.5	5.5	D	.....
					Oligodendroglioma and Ependymona of Filum Only						
102	1	40 M	Pain	Filum	Removal	..	2.5	10.5	13	L	Neurosis

Conus and Filum Terminale Group

Only two astrocytomas involved the conus and filum terminale, as compared with 14 ependymomas. Of astrocytomas that arose from the filum, there were 5, as compared with 21 ependymomas.

Comment

Two patients deserve brief comment. One of these patients, who had an intramedullary astrocytoma, also had multiple sclerosis. The other, a woman, had an astrocytoma removed from the filum and died 30 years later with organic dementia (table 5), as had her father.

On the whole, it could be said of patients who had intramedullary astrocytomas that they got on about as well whether or not the tumor was removed.

MISCELLANEOUS TUMORS OF THE CORD AND FILUM TERMINALE

A prominent feature of the miscellaneous tumors is the larger representation by types than by numbers in any one type. A rapid survey may be made by consulting charts 6 and 7 and tables 5 and 6.

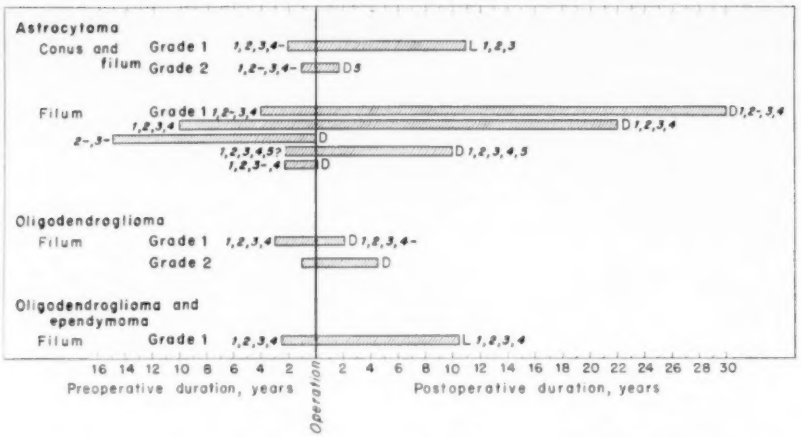

Chart 6.—Duration of symptoms before operation and survival after operation: data in cases of miscellaneous gliomas of the conus and filum terminale (cases 93 to 102 inclusive; table 5).

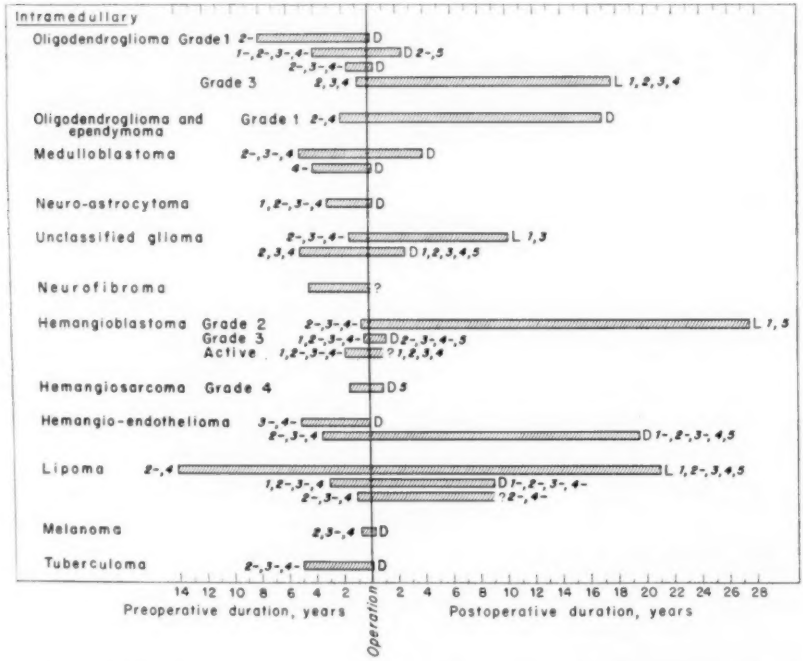

Chart 7.—Duration of symptoms before operation and of survival after operation: data in cases of miscellaneous tumors of the spinal cord, exclusive of the conus and filum (cases 103 to 124 inclusive; table 6).

TABLE 6.—*Miscellaneous Intramedullary Tumors of Spinal Cord Exclusive of Conus and Filum Terminale: Twenty-Two Cases* *

Case	Grade	Age; Sex	Symptoms	Level	Operative Procedure	Roentgen Therapy	Duration, Yr.			L or D †	Comment
							Preoperative	Postoperative	Total		
					Oligodendroglioma						
103 ‡	1	34 M	Weakness; incontinence	Th 10	Subtotal removal	..	8	0.2	8.2	D	Ulcers; septicemia; necropsy
104 ‡	1	40 M	Pain; weakness	C 3-6	Decompression	+	4	2.5	6.5	D	.....
105 ‡	1	29 F	Pain; weakness	Th 4	Removal	..	1.5	0.4	1.9	D	Paraplegia; choked disks
106	3	38 M	Pain; numbness	C 4-5	Removal	..	0.8	17.7	18.5	L	Works; well
					Oligodendroglioma and Ependymona						
107 ‡	1	36 F	Pain; numbness	Th 9-L 1	Decompression	..	2	17	19	D	Paraplegia; tumor grew into muscle; two operations
					Medulloblastoma						
108 ‡	..	38 M	Weakness; numbness	Th 6-9	Removal	..	5	4	9	D	Recurrence; paraplegia
109 ‡	..	20 F	Weakness	Th 8-L 1	Dura opened	..	4	0.2	4.2	D	.....
					Neuroastrocytoma						
110 ‡	..	34 F	Pain	C 5-Th 2	Subtotal removal	..	3	0.5	3.5	D	.....
					Unclassified Glioma						
111	..	28 M	Pain; incontinence	Th 10	Biopsy	..	1.3	10.2	11.5	L	Paraplegia program
112	..	40 F	Numbness; pain	C 1-5	Decompression	+	5	2.5	7.5	D	Worked as nurse; tetanus; paralyzed last few days
					Neurofibroma						
113 ‡	..	12 M	Pain; weakness	C 4-7	Subtotal removal	..	4.3	2 wk.	4.4	?	Improved after operation
					Hemangioblastoma						
114 ‡	2	30 M	Pain; numbness	Th 5	Removal	+	0.5	27.5	28	L	Recurrence; paraplegia regimen
115 ‡	3	32 M	Incontinence; pain	C 1	Subtotal removal	+	0.3	1.2	1.5	D	Foramen magnum; syringomyelia
116	Active	39 M	Numbness; weakness	C 4	Removal	..	1.7	1	2.7	?	"Good health" 1 yr. after operation
					Hemangiosarcoma						
117 ‡	4	34 M	Pain; numbness	Th 2	Decompression	+	1.5	1	2.5	D	Invasion of scar; paraplegia
					Hemangioendothelioma						
118 ‡	..	30 F	Pain; weakness	C 6	Decompression	..	5	1 day	5	D	Fall on ice; short period of paralysis
119 ‡	..	50 M	Pain; numbness	Th 7-8	Biopsy	+	3.5	19.5	23	D	Worked in garden; died from cancer of colon
					Lipoma						
120 ‡	..	19 M	Pain; ataxia	C 6	Subtotal removal	+	14	21	35	L	Holding own
121	..	44 M	Numbness; stiffness	Th 10-11	Removal	..	3	9	12	D	Outcome apparently good; cause of death unknown
122	..	20 F	Pain; numbness	Th 6-8	Biopsy	..	1	9	10	?	Improved after operation; tuberculosis of kidney
					Melanoma						
123	..	49 M	Pain; numbness	Th 6-8	Subtotal removal	..	0.7	0.1	0.8	D	.....
					Tuberculoma						
124 ‡	..	20 F	Pain; weakness	C 5-Th 2	Removal	..	5 (?)	5 days	5	D	Acute meningitis; necropsy; overlying lipoma

DEGREE OF MALIGNANCY

One of the objects of this study was to learn whether or not the grade of malignancy of gliomas of the cord, as determined pathologically, is correlated to the clinical course, as may be learned about gliomas of the brain.[3] This part of our study at first was disappointing to us, since the malignancy of so few of these tumors proved to be grade 3 or 4 that the number in these groups was not sufficient to serve as a basis for the formation of any opinion. This, in itself, may be significant. Gliomas of the cord are not malignant as often as are those of the brain.

It is apparent that the degree of malignancy, as encountered in intramedullary glial tumors, is relative. These tumors rarely metastasize, even to the meninges. Unless a tumor continues to grow upward to invade the brain stem, its effect will be to transect the cord; what it can do beyond this that may not also occur to a patient whose cord has been transected from some other cause, as by injury, is still unknown.

One is accustomed to think of the degree of malignancy in terms of postoperative survival; in one's clinical thinking of malignancy relative to tumors of the spinal cord, it may be more practical to consider it in terms of speed and

TABLE 7.—*Data on Association with Syringomyelia Obtained at Necropsy in Sixteen Cases of Intramedullary Tumors of the Spinal Cord*

	Syringomyelia	
	Present	Not Present
Astrocytoma	1	3
Ependymoma	5	2
Oligodendroglioma	2	0
Hemangioendothelioma	2	1
Total	10	6
	62.5%	

intensity of preoperative invasion. At this time a fair estimate can usually be made of the time of onset of symptoms and the amount of damage done. Estimation of the postoperative activity of a tumor is less easy, particularly if the patient becomes completely paralyzed.

Removal of a malignant tumor is not precluded. It is unsafe, however, to credit to the complete removal of an intramedullary tumor the subsequent well-being of a patient, for in our series are several patients who got on well for many years, although they still carried their tumors.

ASSOCIATION OF INTRAMEDULLARY TUMORS WITH SYRINGOMYELIA

The frequent association of intramedullary tumors with syringomyelia has raised questions that still remain unanswered. Table 7 gives the frequency with which this association could be proved in our series of cases.

SUMMARY

A survey was made of a series of patients who had pathologically verified intramedullary tumors of the spinal cord and gliomas of the intradural portion of the

3. Kernohan, J. W.; Mabon, R. F.; Svien, H. J., and Adson, A. W.: A Simplified Classification of the Gliomas, Proc. Staff Meet., Mayo Clin. **24**:71-75 (Feb. 2) 1949.

filum terminale. The primary purpose was to investigate the duration of the illness and to determine whether or not this could be correlated with the pathological grading of malignancy.

It was noted recurrently that the presence of intramedullary tumors of the spinal cord or glial tumors of the conus and the intradural portion of the filum terminale was not always incompatible with reasonably good health for many years, even when the tumor could not be removed.

Of patients with ependymomas, those who had a tumor in the conus fared worst, with a median period of survival before and after operation of 5.5 years; those with a tumor in the cord at a higher level fared better, with a median survival period of nine years; those with a tumor in the filum terminale fared best, with a median survival period of 13 years.

Patients who had intramedullary ependymomas did better, with a median survival period of nine years, than did those with intramedullary astrocytomas, with a median survival of six years.

Taken as a whole, gliomas of the spinal cord are not as malignant as are gliomas of the brain.

Other observations that were made in the course of this study were as follows: The incidence of intramedullary ependymomas and that of astrocytomas were the same, 26. Of tumors that involved the conus and filum terminale, 14 were ependymomas and only two astrocytomas; and of those that arose from the filum 21 were ependymomas and five astrocytomas. There were five extramedullary astrocytomas, of which four were intradural and one was extraspinal; this one was found under the skin.

In this series of tumors ependymomas occurred about twice as often in men as in women, while astrocytomas affected the sexes about equally; however, the onset of symptoms in each type of tumor was later in the male.

Patients with ependymomas of the conus and filum terminale were the youngest, with a median age of 28 years at time of operation; those who had tumors of the filum were intermediate, with a median age of 33 years at time of operation, and those who had tumors of the cord were the oldest, with a median age of 42 years at time of operation. The reasons for this age incidence invited speculation, but they were not apparent to us.

One patient who had an intramedullary ependymoma had a sister who was afflicted with the same type of tumor; both tumors were situated in the cervical and upper thoracic portions of the spinal cord.

If an intramedullary tumor is well encapsulated, an attempt should be made to remove it, but no undue risk ought be taken.

The value of roentgen therapy could not be assessed.

The greatest risk to life arises from decubitus ulcer and complications incidental to impaired function of vesical and anal sphincters. Now that chemical and antibiotic therapy is available, the danger from infection can be combated with greater vigor and confidence. The contributions of the physical therapist and the urologist to the care of these patients deserve greater emphasis than they have received. It should be remembered that most of these patients return to their homes, and it is after their return that complications arise which result in death.

ABSTRACT OF DISCUSSION

Dr. Ward W. Woods, San Diego, Calif.: I should like to congratulate Dr. Woltman on his large series of cases, particularly in view of the long period since the patients were first seen. How often does one have the opportunity of following a patient 38 years after operation? Unfortunately, I have been unable to follow the 68 cases of intramedullary tumors of the cord which Pimenta and I reported (Arch. Neurol. & Psychiat. **52**:383 [Nov.] 1944). However, from our follow-up studies at the time of the report, we came to exactly the same conclusions as has Dr. Woltman. I believe that these lesions are much more approachable surgically than has been considered possible in the past. Our experience has taught us certain things: One is that, regardless of how hopeless the lesion seems to appear, it is important to decompress the spinal cord completely and to make a vertical incision over the tumor, whether it is invasive or not. In making the vertical incision in the spinal cord in cases of these intramedullary tumors, it is important to preserve the arterial supply. Often the dorsal spinal artery can be saved by gently displacing it. It is important to remember that, in incising the cord, it is wise to make the incision over the posterior column, which clinical examination has revealed to be most involved.

In the past year, I have had a case which demonstrates how these lesions can be approached surgically. A 1 year old child was first seen in 1948. She was hydrocephalic, with an occipitobregmatic measurement of 18¼ inches (47.6 cm.). There was no papilledema. The child was edentulous. Motion of the legs was slight. On gross tests sensation seemed intact. The deep reflexes were increased and there was ankle clonus, but the plantar responses were flexor in type. Roentgenological examination showed widening of the intrapedicular spaces in the lumbar and lower thoracic regions. Injection of ethyl iodophenylundecylate (pantopaque®) revealed a complete block at the level of the conus. A total laminectomy was carried out from the sixth thoracic to the fourth lumbar vertebra, and a large intramedullary lipoma presented along the posterior aspect of the cord. There was no line of demarcation, and I felt that the tumor could not be removed; consequently, I left the dura open, cross cutting it to assure more decompression, and did not touch the superior portion of the tumor. One month later a second stage laminectomy was done, from the third cervical to the sixth thoracic vertebra. At this time the tumor had protruded into the space which had been left at the previous decompression, and the dura had already begun to form a sac, compatible with the enlargement of the cord and of the tumor. At the level of the third cervical segment a free flow of cerebrospinal fluid was encountered from above, although the cord was larger than normal. The vertical chordotomy was not extended above this level. The child, unfortunately, left San Diego and went to Cincinnati, but a report from Dr. E. S. Lotspeich stated that the child now has abdominal reflexes, there is no apparent abnormal growth of the head, the fontanels are closed, the deep reflexes are normal, bladder and bowel control are adequate and no sensory deficits can be detected on gross testing. Of course, I am sure that the child must have some impairment of position sense. The mother wrote me that the child, now 3 years old, is beginning to walk, two years after the decompression of the spinal cord from the third cervical segment to the filum terminale.

The pioneer work in this field by Dr. Woltman and Dr. Kernohan continues to bear fruit.

Dr. Arthur Ward, Seattle: It is only through study of large numbers of cases over a long period that the natural history of such neoplasms can be adequately described.

From a practical viewpoint, one would like to know what the course of any given tumor will be and what type of therapy can best modify that course. Figures such as have been presented obviously can be analyzed in many ways, since the answer obtained from any statistical computation is directly dependent on the question asked. It is thus of interest to determine the percentage of patients alive 10 years after operation in each of the pathological groups, irrespective of the type of therapy. In this series, 41 per cent of patients with ependymoma and 39 per cent with astrocytoma of the cord (exclusive of the conus and filum terminale) were alive at the end of 10 years. Although the 10 year survival rates are the same, the responses of these two types of glioma to surgical therapy differ, in that ependymomas in this location do poorly unless radical surgical removal is carried out, whereas a significant number of patients with astrocytomas (5 of 12) were alive after biopsy only. Ependymomas of the conus and filum terminale had a 10 year survival rate of 30 per cent, while the group of miscellaneous neoplasms in the same location showed a similar survival rate of 50 per cent. Ependymomas of the filum terminale showed a 58 per cent survival rate, which may be related to the fact that a large

number (11 of 19) were removed radically. The poorest survival rate, 27 per cent, was that for the miscellaneous neoplasms of the cord proper, and this is not remarkable in view of the histological types involved.

In assessing the surgical therapy of these neoplasms, regardless of the type of tumor, certain conclusions may be drawn. Of all patients treated by decompression alone, only 14 per cent were alive at the end of 10 years, although the total number thus treated (14) was small. In contrast, 30 per cent treated by subtotal removal, 36 per cent by biopsy alone and 51 per cent by radical removal survived the 10 year period. It is thus evident that subtotal removal is apparently of no greater value than biopsy alone and that neither can compare with the much higher rate of useful recovery obtained by radical removal. The only exception to this are the patients with astrocytomas of the cord above the conus, who apparently did well (or poorly) regardless of what was done, provided the cord was explored. The fact that ependymomas of the conus and filum tend to occur primarily in the younger age groups is perhaps related to the somewhat greater embryonic activity in this region, which may also account for the observation that these patients also fared worst, although actually 50 per cent of patients in whom the tumor was removed were still alive at the end of 10 years.

It is obvious that, even with this large series, the individual groups of cases are still too small to permit of accurate statistical analysis. If other, equally well controlled series were to be combined, accurate data could be obtained to describe more accurately the natural history of each type of neoplasm and the effect on its course of surgical and roentgen therapy.

Abstracts from Current Literature

Psychiatry and Psychopathology

A Transference Phenomenon in Alcoholics: Its Therapeutic Implications. C. L. Brown, Quart. Studies on Alcohol **11**:403 (Sept.) 1950.

The treatment of persons who habitually drink to excess is in general unsatisfactory. Although almost every method of treatment can claim some successes, the author wonders whether the diverse therapeutic procedures which seem to yield favorable results do not have a common denominator.

A conversion experience has often been observed in successfully treated alcoholics. This conversion is best regarded as a transference phenomenon. The alcoholic has an exceedingly difficult time in finding any real, consistent acceptance and understanding. What is essential in treatment is that the experience include the absolute conviction of the patient that he is truly accepted by the therapist.

In order to convey to the patient the fact that he has been accepted, the therapist inquires into the realistic problems of the patient, evincing an interest in them and a willingness to help with their solution. Furthermore, since the attainment of considerable insight by the patient is not always a practical desideratum, the therapist gives fewer interpretations to the alcoholic patient than to some other types.

All alcoholics cannot be treated by this approach. Those most accessible are the ones with either a neurosis or a neurotic character disorder in whom alcoholism is a habitually prominent symptom. The most significant prognostic indication seems to be the degree of reality testing that the patient displays.

Further observations are needed to confirm the views advanced in this communication; the cases studied have been too few to allow statistical analysis, and not enough time has elapsed for the full evaluation of the status of former patients. Brown believes, however, that if these views can be validated the treatment of alcoholism might be furthered by the finding of the common basis of divergent methods of treatment.

Alpers, Philadelphia.

Hereditary Ataxia with Optic Atrophy of the Retrobulbar Neuritis Type, and Latent Pallido-Luysian Degeneration. M. André-van Leeuwen and L. van Bogaert, Brain **72**:340, 1950.

André-van Leeuwen and van Bogaert report on the clinical and histological studies performed on a patient with hereditary spinocerebellar degeneration of Marie. The patient, aged 20 at the time of her death, began to show disturbances of gait at the age of 9 years; her vision was poor during the initial examination at that time. Two years before her death there suddenly appeared a severe disturbance in central vision, in the course of a period of acute deterioration involving both the cerebellar and the optic systems. The visual involvement remained stationary until the patient's death, which followed vascular occlusion in the territory of the anterior spinal artery with softenings at the bulbospinal transition zone.

Histological studies revealed, in addition to the necrosis at the bulbospinal transition zone, degeneration of Goll's column, the ventral spinocerebellar tract and the olivary nuclei. There were atrophy of the dentate, emboliform and roof nuclei of the cerebellum; severe atrophy of the body of Luys, with less pronounced atrophy of the corpora pallida and red nuclei; and degeneration of both optic nerves, limited strictly to the papillomacular bundles.

The authors believe that there is a very close affinity between the hereditary ataxias, familial spastic paralysis and Charcot-Marie-Tooth amyotrophy. The optic nerve atrophy seen in these diseases behaves as an integral part of the neurological hereditary degeneration and may take three forms clinically. First is retrobulbar neuritis with loss of visual acuity, central scotomas and temporal discoloration of the disk, the peripheral part of the visual field being little involved; the involvement of the optic nerve in these instances seems to become arrested. This condition was found in the case reported. In the second form, the optic nerve

atrophy may be rapider in progression and more diffused in extent, so that all useful vision is abolished. The disk is atrophied throughout and there is almost complete demyelination of the optic nerves. A third form of optic nerve atrophy associated with the hereditary ataxias is characterized by more or less severe loss of visual acuity, with concentric restriction of the visual fields, which is slowly progressive. This type has not been described histologically.

FRANKEL, Philadelphia.

Diseases of the Brain

NEUROLOGICAL, OPHTHALMOLOGICAL AND OTOLOGICAL MANIFESTATIONS IN A SUBJECT PRESENTING CRISES OF PAROXYSMAL COLD HEMOGLOBINURIA AND THE PHENOMENON OF AUTOAGGLUTINATION OF THE ERYTHROCYTES. A. LESBROS and J. BIGONNET, Rev. d'oto Neuro-Ophthalmologie **21**:339 (Aug.-Sept.) 1949.

Lesbros and Bigonnet report the case of a man aged 72 who since 1942 had had symptoms of paroxysmal hemoglobinuria on exposure to low temperatures; crises which were not due, as in the classic disease, to sensitization to cold of the erythrocytes were caused by a particular state of the serum, involving the autoagglutination of erythrocytes. In addition, the patient had neurological ocular and auricular symptoms, which have progressed slowly for over one year. His neurological difficulties consisted of changes in the coordination of movements of the legs, accompanied with a decreased achilles reflex in one leg and complete absence of the reflex in the other, and diminution of the vibratory sense. There was also mild involvement of the pyramidal tracts.

The ocular symptoms consisted of diminution of visual acuity, associated with bilateral macular degeneration of the vascular type. The auditory symptoms were connected with distinct bilateral lesions of the internal ear.

The question arises of a causal relation between the otoneuro-ophthalmological symptoms and the blood disease. A categorical answer is impossible, since the patient presented also moderate hypertensive vascular disease with possible vascular changes as a result.

The authors believe that an acceptable explanation can be found in the possibility that a massive agglutination of the erythrocytes is accompanied with small emboli in the peripheral vessels, which, when occurring in the central nervous system and the sense organs, may well accumulate to create the distinct lesions observed in this man.

SJAARDEMA, Los Angeles.

POSTVACCINAL ENCEPHALOMYELITIS IN ADULTS: NOSOGRAPHIC POSITION AS DEMYELINATING DISEASE. S. RIGOTTI, Riv. Neurol. **19**:1-144 (Jan.-Feb.) 1949.

In 1945, when smallpox vaccination of adults was obligatory in the Province of Padua, Rigotti observed two cases of postvaccinal encephalomyelitis. The neurological symptoms in adults differ from those in children. From an extensive review of the literature and from his own observations, he concludes that encephalomyelitis following smallpox vaccination in adults is diffusely disseminated in the brain and in the spinal cord. The disease follows a chronic course similar to that of multiple sclerosis. It is a demyelinating dysergia of the nervous system. In the establishment of dysergia of the nervous system, the age of the patient is a factor of importance. The most important dysergic nervous factor, however, is the effect of a previously administered smallpox vaccine.

J. A. M. A.

IMPORTANCE OF THE FUNDUS IN THE DIAGNOSIS OF THE HYPOPHYSIAL TUMORS. O. HIRSCH, Monatsschr. f. Psychiat. u. Neurol. **117**:236 (April) 1949.

Hirsch discusses the older findings of Uthoff, who believed that papilledema and optic neuritis were frequent concomitants of hypophysial tumors. These apparent associated signs were related to the imperfect examinations of the fundus and visual fields prevalent during Uthoff's time. The older anatomic concepts indicated that the chiasm rested in the sulcus chiasmatis and that therefore an encroaching hypophysial tumor would impinge on the chiasm early, producing pressure symptoms. In reality, the cisterna chiasmatis lies between the sulcus and the chiasm. Therefore, many large tumors which cause ballooning of the sella turcica may not produce ocular manifestations. For example, visual disorders are absent in 50 per cent

of all patients with acromegaly who have an enlarged sella, because these tumors tend to grow toward the sphenoid sinus. Hirsch explains the infrequent occurrence of papilledema on the basis of the relation of the chiasm to the circle of Willis. The anterior arc of the circle lies over the chiasm and when a hypophysial tumor elevates the chiasm the latter is pressed against the anterior communicating artery, which runs horizontally and which has become longer through stretching. The artery gradually lies deeper in the extended chiasmal plate and forms a barrier which does not permit the cerebrospinal fluid to penetrate into the optic nerve sheaths. This may explain why papilledema, optic neuritis or secondary nerve atrophy occurs only in about 3 per cent of cases. Hirsch also believes that this tying off of the chiasm and of the optic nerves by the arterial circle is of greater significance than the stretching of the chiasm and is important in the production of the primary atrophy which is so frequent. This mechanism also explains the gradual development of the temporal or bitemporal defects. The pallor of the disk is more striking on the temporal than on the nasal side, and the maculopapillar bundle is more involved in the tying-off process. Of the 59 cases in which Hirsch operated between 1925 and 1935, the disks were normal in 7, despite temporal hemianopsia and decreased vision. This could be explained by the fact that the tying off occurred posteriorly and a longer period elapsed before changes in the disk occurred. The presence of white disks does not necessarily mean failure of restoration of vision.

PISETSKY, New York.

Diseases of the Spinal Cord

POLIOMYELITIS OF THE NEWBORN. PATHOLOGIC CHANGES IN TWO CASES. J. L. BASKIN, E. H. SOULE and S. D. MILLS, Am. J. Dis. Child. **80**:10 (July) 1950.

The authors give a brief review of poliomyelitis in the newborn and report 2 cases. The first infant reported on was born while his mother was in a respirator, critically ill with poliomyelitis of four days' duration. The first signs of illness developed when the infant was 3½ days old. In the second case, the mother had onset of acute poliomyelitis two days after a normal delivery, and the baby showed changes in the spinal fluid when 5 days old. Both infants died, the first on the seventh and the second on the fourteenth day of life.

A review of the literature revealed no previous case in which prodromes in the infant appeared as early as 3½ days of age. In no reported case had the mother had acute febrile poliomyelitis of four days' duration at the time of birth.

In view of the fact that the minimal incubation period of clinical poliomyelitis is fairly well established as five days, and that immediate isolation of the infant in the first case was carried out on delivery, his illness appeared either after an incubation of only three and one-half days or resulted from an intrauterine infection. On the basis of this evidence, it is no longer possible to assume that newborn infants are immune to poliomyelitis.

ALPERS, Philadelphia.

PHYSIOLOGIC SECTION OF NERVE ROOT; SPONTANEOUS RECOVERY PROCESS IN CERTAIN SCIATICAS. J. A. CHAVANY, P. JANNY and D. HAGENMULLER, Presse méd. **57**:773 (Aug. 27) 1949.

Chavany and co-workers report the case of a man aged 39 with bilateral sciatica. The first attack occurred in 1944, without any trauma. There were two recurrences, in 1946 and in 1947. Pain was severe on the right side in all three attacks. In December 1948 the patient had severe influenza, followed by another recurrence of lumbar pain radiating to the leg, but this time mainly on the left side. Both legs felt heavy. The achilles reflex was absent on both sides. Bilateral surgical intervention was carried out by interlaminar approach on the fifth lumbar and first sacral vertebrae. There was herniation of the intervertebral disk on both sides. The nerve root against which the disk protruded on the left side was stretched and adherent. The freeing of it was difficult. The root of the first sacral nerve on the right side was flattened, atrophied, laminated and adherent. The pale and thin nerve root was physiologically deficient with regard to transmission of painful impulses. It could be pinched without producing painful sensation in the lower extremity. Pulling in the course of the operation caused a partial tear of the friable tissue of the nerve root, but this was not accompanied with pain. Physiological division of the root, which had been compressed for a long time by the

voluminous disk, was responsible for the spontaneous and definite recovery from the sciatic pain on the right side. The residual analgesia emphasizes the fact that all cases of chronic sciatica subside eventually without leaving the patient permanently crippled. This is also true of the protracted cases of sciatica with recurrences.

J. A. M. A.

CONTRALATERAL RECURRENT HERNIATED DISKS. HENRY WYCIS, Arch. Surg. **60**:274 (Feb.) 1950.

Ruptured intervertebral disk not infrequently causes bilateral symptoms, which may occur alternately or simultaneously. The change of symptoms may be due to a midline or to a bilateral herniation of the disk. On occasion, contralateral symptoms and signs are observed in cases of unilateral rupture of a disk. The author reports four cases in which contralateral sciatic pain was produced by recurrence of herniated disk at the same interspace after surgical removal of the lesion. In three cases reoperation on the contralateral side relieved all symptoms, and in the fourth case the recurrent lesion had not yet been verified. A fifth observation is reported in which ipsilateral symptoms were relieved by contralateral removal of a partially herniated disk. Experiences of this type may influence neurosurgeons to perform a more complete laminectomy than is at present customary. At any rate, the suspected interspace should be explored on both sides.

LIST, Grand Rapids, Mich.

OBSERVATIONS ON INFANTILE PARALYSIS. L. BARRAQUER-FERRE and E. CASTANER-VENDRELL, Rev. españ. pediat. **6**:359 (May-June) 1950.

Barraquer-Ferre and Castaner-Vendrell studied 2,050 cases of poliomyelitis. They point out that the lesions of poliomyelitis are observed consistently in the anterior horn cells but may appear rarely in other areas. They state that they have never seen a death from cerebral involvement in poliomyelitis, all their deaths resulting from bulbar forms. In none of their cases was spasticity of the muscles observed. They found that warm baths and passive movement during immersion were useful in early treatment, together with postural care and electrotherapy. Chemotherapy was of no value; neither was whole blood from parents or from persons who had previously had the disease.

ALPERS, Philadelphia.

Peripheral and Cranial Nerves

VESTIBULAR FINDINGS BEFORE, DURING AND AFTER VESTIBULAR DAMAGE RESULTING FROM STREPTOMYCIN THERAPY. JULIUS WINSTON, Arch. Otolaryng. **47**:746 (June) 1948.

Winston reports on three patients treated with streptomycin. Two of these patients had vestibular examinations at frequent intervals before, during and after therapy. When vestibular damage began to occur, the duration of nystagmus after turning was decreased, and there was also a decrease in duration of vertigo in response to turning. A third case was reported in which there was no response to turning; but since no vestibular examinations were made before the administration of streptomycin, these results were not conclusive. In none of the cases was there any impairment of hearing.

There is a disproportionate reduction in the responses of nystagmus and vertigo which would support the hypothesis that the lesion is central or that there are in the ampullae two separate sets of hair cells for picking up the impulses producing nystagmus and for those eliciting vertigo, respectively.

RYAN, Philadelphia.

MÉNIÈRE'S SYNDROME; OBSERVATIONS ON VITAMIN DEFICIENCY AS THE CAUSATIVE FACTOR: II. THE COCHLEAR DISTURBANCE. MILES ATKINSON, Arch. Otolaryng. **50**:564 (Nov.) 1949.

In this, the second, portion of a report on observations on vitamin deficiency in Ménière's disease, Atkinson deals with the cochlear disturbance, or chronic phase. Perceptive deafness was the commonest variety of hearing loss. Pure conduction deafness was noted in a small percentage of cases but was oftener combined with perceptive deafness. Observations suggested that the factor responsible for the lesion causing perceptive deafness is niacin deficiency and

the factor responsible for the lesion causing conduction deafness is riboflavin deficiency. It was further found that patients in whom perceptive deafness predominates complain predominantly or solely of rotational vertigo, whereas those in whom conduction deafness predominates complain predominantly or solely of positional vertigo. When the conduction type of deafness was present, the hearing loss was severer. This would indicate that riboflavin deficiency, if this is the responsible factor, gives rise to a severer disturbance than does niacin deficiency. To corroborate this further it was found that the best responses to treatment were obtained in the niacin-deficient group and the poorest responses in the riboflavin-deficient group.

After classification of the various types of tinnitus, it was found that patients having perceptive deafness more frequently had a steady type of tinnitus and those having conduction deafness had a rhythmic type. Mixed types of tinnitus were also associated with mixed deafness, suggesting that each type of deafness has its own type of tinnitus. In these studies on tinnitus, confirmation is again made of the observation that riboflavin deficiency produces a severer type of disturbance than does niacin deficiency. The response to treatment was more encouraging in regard to tinnitus, and here, again, the best results were obtained in the niacin-deficient group.

The suggestion is made, on physiological grounds, that by including the cochlea with the external auditory apparatus as part of the anatomic mechanism of conduction deafness, one can account for the symptoms due to specific vitamin deficiencies in Ménière's syndrome.

RYAN, Philadelphia.

THE ANTERIOR ETHMOIDAL NERVE SYNDROME: REFERRED PAIN AND HEADACHE FROM THE LATERAL NASAL WALL. HOWARD H. BURNHAM, Arch. Otolaryng. **50**:640 (Nov.) 1949.

The anterior ethmoidal nerve syndrome is the name suggested for a series of symptoms resulting from irritation of the terminal branches of the anterior ethmoidal nerve. The referred pains in this syndrome are chiefly pains of the sinus type or headache, occasionally of a migrainous nature. Application of ephedrine to the anterior ethmoidal fissure and/or the middle turbinate body has brought relief in many cases. Burnham describes a persistent case in which relief was finally obtained after severance of both anterior ethmoidal nerves.

RYAN, Philadelphia.

Treatment, Neurosurgery

EFFECT OF STREPTOMYCIN ON TUBERCULOUS MENINGITIS. H. D. BRAINERD and H. R. EAGLE, Ann. Int. Med. **33**:397 (Aug.) 1950.

Twenty-seven patients with tuberculous meningitis were studied to determine the effect of streptomycin on the course of the disease. The intramuscular and intrathecal doses of streptomycin varied considerably. An attempt was made to treat all patients for five months by the intramuscular route. Intrathecal treatment was administered according to several plans.

The patients fell roughly into five groups, according to the course of the disease under treatment. 1. Nine patients died during the first four weeks of treatment without significant clinical or laboratory evidence of improvement. 2. Eight patients showed initial favorable clinical and laboratory response but later relapsed and died while still receiving treatment. These patients all survived more than eight weeks but died before the end of the five month therapy period. 3. Two patients showed initial favorable clinical and laboratory response but maintained slight persistent evidence of infection after completion of the five month therapeutic period. They died seven and 12 months, respectively, after the onset of meningitis. 4. One patient was free of all evidence of infection of the central nervous system after the completion of five months of treatment, but meningitis recurred 100 days later. 5. Six of the 27 patients are alive, from 18 to 31 months after the institution of treatment. Of the survivors, two manifest moderate residual neurological damage, and a third has had three grand mal seizures but is otherwise entirely normal.

Brainerd and Eagle point out that most patients having a favorable response to treatment received more than 60 mg. of streptomycin daily per kilogram of body weight intramuscularly

and over 2.0 mg. per kilogram daily by intrathecal injection. Toxic reactions to streptomycin are frequent at high dose levels but are a justifiable risk. In spite of current therapy, the prognosis of tuberculous meningitis must still be considered very grave.

ALPERS, Philadelphia.

AUREOMYCIN IN STAPHYLOCOCCIC MENINGITIS COMPLICATING SUBARACHNOID HEMORRHAGE IN SICKLE CELL ANEMIA. J. R. ALMKLOV and A. E. HANSEN, Pediatrics **3**:764 (June) 1949.

Almklov and Hansen report the occurrence of a spontaneous subarachnoid hemorrhage in a Negro boy aged 11 years with sickle cell anemia. Of the 8 cases mentioned in the literature, 5 have occurred in children. In the study of sickle cell anemia there is an increasing awareness of subarachnoid hemorrhage and other neurological complications, such as hemiplegia, coma and convulsions. In the authors' case there developed meningitis due to Staphylococcus albus, which for twelve days resisted combined treatment with penicillin, streptomycin and sulfadiazine. Treatment was discontinued; because the patient's prognosis seemed hopeless, it was thought justifiable to exhibit an experimental antibiotic agent. The patient was given 20 mg. of aureomycin intramuscularly every eight hours. Within two days he improved remarkably and was taking fluids by mouth. After five days the spinal fluid revealed only 5 cells per cubic millimeter; no organisms were seen on smear, and cultures were sterile. Aureomycin was given for a total of 10 days, by the end of which time the patient had become alert and could recognize persons. There were no untoward reactions to the intramuscular administration of the drug. In vitro studies disclosed that when penicillin and aureomycin or streptomycin and aureomycin were combined, the result was a decrease in the effectiveness of either drug against staphylococci. The feature which probably played a role in the excellent response of the patient to aureomycin therapy was the decision to discontinue the use of all other therapeutic agents. More effective results in the treatment of staphylococcic infections may be obtained if aureomycin is used as the sole antibiotic agent.

J. A. M. A.

Muscular System

SURGICO-PATHOLOGICAL ASPECTS OF MYASTHENIA GRAVIS. H. REID, Brit. J. Surg. **36**:381 (April) 1949.

Reid reports six cases of myasthenia gravis in which he removed the thymus or a tumor. Four cases were associated with a "persistent" thymus, one with a malignant thymoma and one with an innocent thymoma. The patient with the malignant thymoma, who had severe myasthenia gravis, died after surgical removal of the tumor. The patient with the benign thymoma and severe myasthenia was much improved at the time of the report, three months after the operation but had not yet returned to work. Three years after operation, three of the four patients with persistent thymus were back at full work with few or no symptoms. One had had a recurrence and required regular doses of neostigmine.

J. A. M. A.

Encephalography, Ventriculography and Roentgenography

CEREBRAL ARTERIOGRAPHY. R. E. WISE, C. R. HUGHES and J. R. HANNON, Am. J. Roentgenol. **64**:239 (Aug.) 1950.

This paper is based on a review of 150 arteriograms. A tumor can be localized by means of vascular displacement. The vascular pattern of a tumor (called tumor "stain") may be characteristic of its pathological type. Tumors of the frontal lobe generally show displacement of the anterior cerebral artery across the midline to the opposite side. Frequently the middle cerebral group is displaced downward and the carotid siphon downward and backward. Tumors of the anterior parietal area may displace the anterior cerebral artery across the midline; a posterior parietal mass will push the callosal branches across the midline. The middle cerebral group may be displaced downward. Tumors of the temporal lobe characteristically elevate the middle cerebral vessels and may straighten the carotid siphon. Tumors of the occipital lobe are infrequent. Upward displacement of the terminal third of the middle cerebral group and the

pericallosal artery has been described. Tumor "stain," or the vascular pattern, when present, is of diagnostic value. "Stains" have been described as characteristic of meningioma, glioblastoma and oligodendroglioma.

Congenital arteriovenous malformations (angiomas), arteriovenous fistulas and aneurysms all lend themselves well to visualization by arteriography.

In one case failure of the middle cerebral artery to fill confirmed a clinical diagnosis of thrombosis of this vessel. However, failure of a vessel to fill must be evaluated with caution.

The authors conclude that cerebral arteriography is a valuable adjunct to air studies and causes less discomfort to the patient. Of 38 tumors, 12 were localized by arteriography alone, five more accurately than by air studies. Arteriography is the only accurate method of demonstrating intracranial aneurysms, arteriovenous fistulas and arteriovenous anomalies.

TEPLICK, Philadelphia.

NON-SIGNIFICANT VENTRICULAR SHIFT IN PNEUMOENCEPHALOGRAMS, WITH PARTICULAR REFERENCE TO THE BOWING OF THE SEPTUM PELLUCIDUM. D. C. Eaglesham, Radiology **55**:1 (July) 1950.

Eaglesham observed that ventricular shifts may appear in the encephalogram in the absence of space-occupying or atrophic lesions. The representative cases of this nonsignificant shift fell into three broad groups: (1) cases with unequal filling of the lateral ventricals; (2) cases of the shift associated with subdural gas, and (3) cases in which the shift is encountered in the follow-up examination after 24 hours or more.

In cases of unequal filling of the ventricles, the clue to the nature of the shift lay in the bowing of the septum pellucidum. If this structure was found bowed with the convexity toward the less filled ventricle, the shift was regarded as artificial. Further manipulation of the head might lead to better filling of the ventricle, and there would no longer be a shift on the film. In the second group, subdural gas, if sufficiently large, was found to produce depression, distortion and narrowing of the homolateral ventricle and a fairly sizable ventricular shift to the opposite side. In this type of nonsignificant shift there was no bowing of the septum pellucidum. In the third group, when follow-up encephalograms were made after 24 or 48 hours, not infrefrequently the ventricles were not symmetrically filled at this period, and there was often a shift, with bowing of the septum pellucidum.

The exact mechanism of this delayed shift is uncertain, but its recognition tends to decrease inaccurate interpretation.

TEPLICK, Philadelphia.

Cerebrospinal Fluid

THE LUMBAR CEREBROSPINAL FLUID PROTEIN IN INTRACRANIAL MENINGIOMAS. W. E. STERN, Brain **73**:72, 1950.

Stern analyzed the spinal fluid protein values obtained in a series of verified cases of intracranial meningiomas in order to determine the relation between the anatomic site of the tumor and the protein value. Significantly higher protein values were found in cases of involvement of the olfactory grove and outer third of the sphenoidal ridge when these were compared with values for meningiomas in other sites. A high value is not likely to come from a meningioma of suprasellar or falcial location. The source of the increased protein has not been found.

FRANKEL, Philadelphia.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Joseph A. Luhan, M.D., President in the Chair
Regular Meeting, Oct. 10, 1950

Differential Diagnosis and Treatment of Certain Nonconvulsive Forms of Epilepsy. DR. FREDERIC A. GIBBS.

At least a third of all epileptic seizures are nonconvulsive. This is not surprising, because a large part of the brain has no motor function. Motor components do not appear in an epileptic seizure until the seizure discharge reaches motor areas.

Seizures associated with one or more of the following symptoms, namely, blinking the eyes, nodding the head, staring and impairment of consciousness are particularly common in children. They constitute what is called a petit mal or pyknoleptic, attack. This type of disorder has long been distinguished as a separate diagnostic entity. It is associated with 3 per second wave and spike discharges and is best treated with trimethadione U. S. P. (tridione®) or paramethadione (paradione®).

Recent studies have made it possible to separate a new diagnostic entity from the general group of seizures referred to as epileptic equivalents. This new entity is termed psychomotor epilepsy. Although convulsions are common in this condition, the outstanding feature of the seizure is trancelike, confusional behavior. When these attacks are very brief, they may be difficult to distinguish from seizures of the petit mal type. However, auras and more or less elaborate, apparently purposeful movements, such as groping, fumbling and smacking of the lips, do not occur in petit mal epilepsy, but they are common in psychomotor epilepsy.

Experience has shown that trancelike, confusional episodes correlate as highly with an epileptic process in the anterior temporal region as a jacksonian type of sensory or motor march correlates with seizure activity in the central area. Psychomotor epilepsy is associated with a focus of seizure activity in the anterior temporal region, and it is the commonest type of focal epilepsy. That the trouble is actually in the temporal lobe has been demonstrated by Dr. Percival Bailey and Dr. John Green, both of whom have performed temporal lobectomies for psychomotor epilepsy. Removal of the anterior third of the temporal lobe (anterior to a line continued down from the central sulcus) usually eliminates the seizure discharge and does not reveal any residual primary focus in the remaining cerebral or the thalamic structures. Postoperative recording in these cases, as well as recordings from the depths of the brain with needle electrodes, gives no evidence that the discharge from the temporal lobe arises anywhere except from the anterior portion of the temporal lobe. The discharge may arise, however, from the medial, anterior, inferior or lateral surface of the anterior third of the temporal lobe.

Although patients with psychomotor epilepsy are more resistant to anticonvulsant medication than patients with grand mal seizures only, all available anticonvulsant medication should be tried. The anti-petit-mal substances trimethadione and paramethadione are rarely effective in psychomotor epilepsy but may be tried in cases in which the disease is resistant to diphenylhydantoin, phenobarbital and methylphenylhydantoin (mesantoin®). Operation is recommended only in those cases with severe psychomotor seizures which are not controllable with maximal tolerated doses of anticonvulsant medication.

The clinical syndrome of thalamic and hypothalamic epilepsy has been recognized for many years. Recently it has been found that 14 and 6 per second positive spikes appearing in the electroencephalogram during light sleep correlate highly with epileptic symptoms referable to the thalamus and hypothalamus. Convulsions occur in approximately 50 per cent of such cases, but more prominent in these cases are attacks of pain, rage, dizziness or prolonged

fainting without convulsive movement of any type. Ictal vasomotor and visceromotor symptoms are common. During the attack cortical activity is usually normal. The patient does usually not appear to be confused; the rage attack of a patient who shows 14 and 6 per second activity in light sleep is highly purposeful, well directed and precisely coordinated. Of 300 patients studied, four have committed murder. This is a much higher incidence than is encountered among patients with psychomotor epilepsy, in which although assaultiveness is common, the patient behaves as though he were acting out a bad dream. The clouded mental state and motor incoordination of the patient with psychomotor epilepsy usually make him fairly easy to handle.

Fortunately, the seizures which occur in patients with 14 and 6 per second positive spikes are, as a rule, readily controlled with diphenylhydantoin, phenobarbital and methylphenylethylhydantoin. In fact, such seizures appear to be more sensitive to anticonvulasnt medication than any other type of epileptic seizure. This is a common type of disorder, but when unassociated with convulsions it is usually misdiagnosed as hysteria, organic neurosis, gastric migraine or appendicitis.

The commonest etiologic factor in cases of thalamic and hypothalamic epilepsy is head trauma. This might be assumed to reflect merely the commonness of head injuries in all persons. However, we believe that trauma is a significant etiologic factor in patients with 14 and 6 per second positive spikes, because it is rarely present in patients with petit mal epilepsy and is relatively uncommon in persons with psychomotor epilepsy.

Mixed types of seizures are frequently encountered, but the fact that petit mal seizures are common in children and psychomotor seizures are common in adults 30 to 40 years of age means that these two types of disorder are not usually concurrent. (Petit mal, however, does not tend to change into psychomotor epilepsy with increasing age.) Fourteen and 6 per second positive spikes are rarely encountered with petit mal. However, grand mal seizures are commonly associated with other types of seizure; to be specific, about one half of all patients with petit mal seizures, with psychomotor seizures or with 14 and 6 per second positive spikes have grand mal seizures also. A mixture of petit mal and grand mal poses a difficult therapeutic problem, for trimethadione, which is the most effective anti-petit-mal substance, tends to aggravate the grand mal disorder, and diphenylhydantoin, which is a highly effective anticonvulsant, tends to increase the petit mal disorder. In cases of this type a new, but somewhat toxic, substance called Phenurone (phenacetylurea) may solve the problem, for it is effective in both types of seizure.

DISCUSSION

DR. FREDERIC GIBBS: I shall answer the questions in the reverse order of that in which they were asked.

Dr. Luhan's question can be answered only with a guess, because most of the patients my colleagues and I see in our epilepsy clinic are referred to us with the complaint of "convulsions." However, of the 300 patients in whom we found 14 and 6 per second positive spikes, only one-half had a history of convulsions. In only one fourth of these were the convulsions a prominent feature of the history. The outstanding symptoms were usually referable to functions which are generally considered thalamic or hypothalamic.

It must be remembered that a convulsion occurs when the discharge spreads to involve the entire brain. Just as convulsions are likely to be associated with sensory seizures of the jacksonian type, so convulsions can be expected as a manifestation of spread from a strong thalamic or hypothalamic epileptic discharge.

Now that trimethadione is being increasingly used by practitioners, consultants see fewer and fewer patients with uncomplicated petit mal. Likewise, fewer patients with pure grand mal are referred to a specialized center, as the new anticonvulsants are used increasingly by general practitioners. It is difficult, therefore, to give any valid figures on the absolute and relative incidences of the different types of epilepsy. However, I would venture a guess that one fourth of all epileptic patients have petit mal, one-fourth grand mal, one-fourth psychomotor seizures

and one-fourth seizures referable to the thalamus or the hypothalamus. However, one-half the patients with each of these types of seizures will probably be found to have a combination of seizures.

Dr. Mackay's question is one of terminology and semantics. It seems to me inadvisable to compartment one's thinking. One should not talk, on the one hand, about a clinical syndrome and, on the other, about electroencephalographic findings. Both are evidences of disorder; we are trying to look through the manifestations at the disorder itself.

The clinician may have what he considers valid evidence of gallbladder disease. The pathologist also has what he considers valid criteria of gallbladder disease. When the clinical symptoms are present and the anatomicopathological evidence is absent, there is reason for argument and discussion. The two sets of evidence should be reconcilable; it does not help to say that the two specialists are talking about different things. The electroencephalographer and the clinician are talking about the same thing.

We believe that if the clinical concepts are refined and altered slightly they will be found to fit very well with the electroencephalographic findings. If, however, the clinical classification of epilepsy is dialectic and no effort is made to adjust it to the facts revealed by physiological study, a permanent impasse develops between the laboratory and the clinic. As an epileptologist, I believe that a barrier between the clinic and the laboratory is artificial and undesirable. I cannot agree that the clinician is entitled to describe a disorder without reference to the laboratory findings, any more than I believe that it is reasonable for the laboratory worker to describe his findings without reference to the clinical symptoms. The barrier between the clinician and the laboratorian has broken down in other fields—in roentgenography an area of opacity is described as a mass, and in cardiology a prolonged QRS complex is described as a bundle branch block. It is now 14 years since my colleagues and I described the 3 per second wave and spike activity which correlates so highly with petit mal epilepsy. As experience has increased and special remedies have been developed for this specific disorder, it has become increasingly reasonable to speak of the 3 per second discharge as a petit mal discharge, provided, of course, that one recognizes that epilepsy may be clinical or subclinical.

In my opinion, the electroencephalographer has the responsibility of fully informing the clinician who consults him regarding the clinical correlates and the therapeutic indications of his findings. He can do this best by speaking the clinician's language, which, after all, is a good language. However, in the nature of things, as new knowledge develops, the clinician and the electroencephalographer will have to agree to modify old terms and coin new ones.

Angiography in Diagnosis of Tumors of the Posterior Fossa. DR. OSCAR SUGAR.

Though most tumors of the posterior fossa and brain stem are relatively easily diagnosed from the clinical symptoms, there is sometimes considerable difficulty in differentiating such tumors from vascular disease. This is particularly true when there is no increase in intracranial pressure. In other cases the tumor produces a clinical picture which may be so atypical as to suggest hysteria. Ventriculography is not always helpful, especially when the third ventricle and aqueduct are not filled with air. In still other instances it would be of advantage to know the exact locus of a tumor or to have some idea of its type or its major sources of blood supply before operation. For these reasons, percutaneous vertebral angiography may be used, sometimes with excellent results. The resulting pictures may reveal displacement of large vessels or give discrete outlines of the tumor, as well as show vascular patterns which may aid in differential diagnosis. The chief sign of increased pressure in the posterior fossa is straightening of the vertebral-basilar system, which is pushed near the clivus and dorsum sellae. This is analogous to the narrowing or disappearance of the pontile and interpeduncular cisterns in pneumoencephalograms. Angiograms have been obtained showing changes associated with the following neoplasms: carcinomatous metastasis to the thalamus, glioma of the thalamus, pinealoma, acoustic neuroinoma, metastases to the pons, glioma of the pons, astrocytoma of the medulla oblongata, ependymoma of the fourth ventricle, cerebellar astrocytoma, metastasis to the cerebellar hemisphere, meningioma of the cerebellum, cystic and solid hemangioblastomas of the cerebellum, cerebellar sarcoma and meningioma of the region of the foramen magnum.

DISCUSSION

DR. HARRY MAXWELL: What are the measurements from the basilar artery to the clivus in normal persons?

DR. OSCAR SUGAR: One-half centimeter or more. The measurements are given with some detail by Davidoff and Epstein (Abnormal Pneumoencephalogram, Philadelphia, Lea & Febiger, 1950), for they correspond fairly well with the distance from the pons to the clivus and dorsum sellae in air studies.

DR. MOORE: What are the untoward effects of vertebral angiography?

DR. OSCAR SUGAR: In one patient with severe arteriosclerosis of the basilar artery the additional vasoconstriction due to the iodopyracet injection U. S. P. (diodrast®) caused ischemia of the brain stem and death. This is the only death directly attributed to this type of angiography. One patient early in our series had a Brown-Séquard syndrome, presumably as the result of the needle entering the spinal canal through the intervertebral foramen. Since that time we have learned to direct the needle always anteroposteriorly without turning it toward the midline and have had no further occurrences similar to this. I am told that there have been three such accidents in England, which have made British workers rather chary of making vertebral arteriograms.

Although a 17 gage needle is used to puncture the artery, I know of no instance of hematoma or other bleeding of importance.

DR. MOSES ASHKENAZY: Are the contraindications of List and Hodges still valid in vertebral angiography, namely, that the test is contraindicated with very old people and in cases of advanced arteriosclerosis, hypertensive vascular disease, cardiac decompensation, recent embolic or thrombotic episodes and acute intracranial hemorrhages?

DR. OSCAR SUGAR: To the best of my recollection, these contraindications were those for carotid angiography, since these authors had done very little vertebral work. So far as I know, there is no contraindication in the presence of emboli or thrombi. Persons with cardiac decompensation certainly should not have such a procedure, and if the diagnosis of cerebral arteriosclerosis were made, and this is very difficult to make, it would be best and safe to use a colloidal suspension of thorium dioxide (thorotrast®), even though this carries some risk of radioactivity. It is because of this that, in general, in the case of patients past the age of 50 or 55 we use thorotrast® for angiography.

Hemangioblastoma and Lindau's Disease. DR. BEN W. LICHTENSTEIN.

The problem of hemangioblastoma and Lindau's disease is comparable to that of neurofibromatosis and von Recklinghausen's disease of the nervous system. The hemangioblastoma is a specific type of connective tissue tumor found almost exclusively in relation to neural elements. Although isolated lesions, termed hemangioblastomas, have been described in the skin, kidney and elsewhere, the historical picture of these lesions is not identical with that of the classic cerebellar tumor in Lindau's disease. The classic triad of Lindau's disease, or von Hippel-Lindau disease, namely, angioma of the retina, solid or cystic hemangioblastoma of the hindbrain (especially the cerebellum) or spinal cord and cystic adenomas of the kidneys, is well known. To these one may add the angiomas of the liver, the cysts of the pancreas and, in rare instances, the tumors of the epididymis which may be described as reticulomas.

The hemangioblastoma is composed of two basic components: reticulum cells, having a great tendency to store lipid substances, and endothelium-lined spaces. These two elements may coexist or occur independently, with certain local modifications. Although "hemangioreticuloma" and "hemangiohistiocytoma" are more descriptive, the term "hemangioblastoma" is too firmly entrenched in the literature to be discarded.

The parenchyma of the kidney arises from mesenchymal tissue and differentiates into two basic elements—blood vessels and intervascular or perivascular cells having modified histiocytic properties. The lining of Bowman's space in the fetal glomerulus is cuboidal epithelium and is analogous to the cells of the renal tubules. Tumors of these cells appear epithelial in spite of their mesenchymal origin and have been designated as adenomas or hypernephromas of the kidney. These frequently become cystic and correspond to tumors of the intervascular cells

or reticulum cells of the hemangioblastoma. In other portions of the kidney, large endothelium-lined spaces occur, corresponding to the vascular component of the kidney. That these lesions arise from embryonic defects in development is emphasized by the finding of a fetal glomerulus and islands of undifferentiated embryonic kidney tissue.

The lesions in the pancreas are cysts with an indistinct lining surrounded by collagenous connective tissue. It is my belief that these represent lymphangiomatous cysts. It thus appears that the formula for all the lesions in Lindau's disease is rather uniform, namely, endothelium-lined spaces and tumors of reticulum cells assuming different shapes in different organs. Many times, the pathologist finds difficulty in differentiating a primary hemangioblastoma of the cerebellum from a metastatic hypernephroma to the cerebellum. In the light of the foregoing discussion, the similarity between these two lesions is evident.

DISCUSSION

DR. NORMAN B. DUBIN: Most of the symptoms presented by the first patient were due to an intracranial lesion. In view of the pathologic process in the pancreas reported, did this patient show any clinical or laboratory signs of pancreatic dysfunction?

DR. BEN W. LICHTENSTEIN: This patient was hospitalized elsewhere, and I have not followed his clinical course. From the records available, there was no clinical evidence of pancreatic involvement.

Accuracy of Preoperative Electroencephalographic Localization in Neurosurgery. DR. LUIS V. AMADOR.

In this study, 297 verified cases of brain tumor were analyzed. The patients had progressive neurological deficit or progressive symptoms and were therefore considered "brain tumor suspects." Standard eight channel electroencephalography was carried out as part of the preoperative work-up. All of the diagnoses were verified at operation or by autopsy. In the neurological cases (83) in this series not only complete studies but also long-term follow-up observations, averaging two to three years, were made in the clinic.

Accuracy is difficult because it varies with the location and histologic character of the tumor, the arbitrary standard used and the intensity of the electroencephalographic study. These factors account for the diversity of opinion among those who have studied this subject. The lesions have been divided into cortical, cerebellar, deep midline and nonsurgical, and the accuracy of localization has been estimated on this basis.

Location	Correct	Total	Percentage
Cortical	121	144	84
Cerebellar	15	25	60
Deep	13	45	29
Nonsurgical	60	83	72
Total	209	297	70

In this series, there were 185 neoplasms. Other lesions included nonsurgical lesions, abscesses, subdural hematomas and aneurysms. It is apparent that the greatest accuracy of the electroencephalogram was obtained with cortical abscesses, glioblastomas and astrocytomas. Deep midline lesions revealed abnormal diffuse changes compatible with deep tumors in only 29 per cent of cases. In children, and more rarely in adults, cerebellar tumors may be manifested by a bioccipital slow wave focus.

In summary, one may state that the accuracy of the electroencephalogram varies with the location and type of the lesion. Cortical lesions are localized much better than those of the cerebellum or lesions deep in the brain. Used intelligently, electroencephalography is an important addition to the armamentarium of the neurosurgeon.

DISCUSSION

DR. M. ASHHUGG: My colleagues and I have studied 340 patients at the Veterans Administration Hospital at Hines and at Passavant and Wesley Hospitals who were suspected of having tumor and have correlated the results of our radiopaque dye study with those of

electroencephalography. Our electroencephalographic reports are also under the supervision of Dr. Gibbs. However, our results have not been nearly as accurate as those reported by Dr. Amador. We have had only 45 per cent accuracy with focal lesions and 60 per cent accuracy with diffuse changes.

Courville, of Los Angeles, also found it difficult to localize meningiomas in cases in which there appeared to be a local quiescence, or malignant tumors, when the widespread abnormal potentials varied so much as to make them difficult to evaluate at times. He, too, found precise electroencephalographic localization only with nonprogressive lesions, such as focal scars, or with benign lesions, such as astrocytomas. He also noted evidence of distinct aberrations which were due to the circulatory and structural reactions of the tumor, the effects of distortion and dislocation of the brain, the degree and acuteness of ventricular distention in whole or in part, the distant effects of pressure (counterpressure) and the transmission of impulses via commissural and associational pathways. Widespread variations in the electroencephalogram also occurred as a result of coma, hydrocephalus, multiple lesions and malignant tumors. Several other investigations revealed slow wave foci over the occipital lobes in cases of tumors of the posterior fossa, and Davidoff and Gibbs found frontal disturbances with cerebellar tumors, just as we have in our series.

News and Comment

THE AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

The following candidates were certified at a meeting of the Board in New York, December 1950.

Psychiatry.—William Colbert Adamson, Philadelphia; Robert W. Allen, Sunnyside, N. Y.; Milton H. Anderson Jr., Ingleside, Neb.; Richard W. Anderson, St. Paul; David C. Asselin, Lansing, Mich.; Louis A. Azorin, Los Angeles; Julian I. Barish, New York; Joseph Lawrence Bell, Lyons, N. J.; Irving Norman Berlin, San Francisco; Herman F. Boerner Jr., Philadelphia; Harold M. Boslow, Perry Point, Md.; Maxwell R. Brand, New York; I. William Brill, Great Neck, N. Y.; Eugene B. Brody, New Haven, Conn.; Richard W. Burnett, New York; Charles K. Bush Jr., Dixon, Ill.; Kenneth Thomas Calder, New York; Walter E. Campbell, Providence, R. I.; Hyman Caplan, New York; Hubert Alfred Carbone, Norwich, Conn.; Russell N. Carrier, Astoria, N. Y.; Leon Harold Caviness, Worthington, Ohio; Frank A. Cellar, Detroit; John S. Clapp, Erie, Pa.; Henry Jonathan Climo, New Orleans; Orris W. Clinger, Warren, Pa.; Felix Cohen, Brookline, Mass.; Elma Margaret Comer, Brooklyn; Frank Whitney Countryman, Topeka, Kan.; George E. Crane, New York; Albert Victor Cutter, Louisville, Ky.; Charles C. Dahlberg, New York; Herman G. DeCherney, Farnhurst, Del.; Chester Roy Dietz, Philadelphia; Merrill T. Eaton Jr., Kansas City, Kan.; John J. Eberhart, Philadelphia; Morton S. Eisenberg, Bronx, N. Y.; Hugo Engel, Bronx, N. Y.; David M. Engelhardt, Brooklyn; Louis Carroll English, New York; Frank Fraser Evans, Chicago; George Sergei Evseeff, Royal Oak, Mich.; Sidney Fine, Beverly Hills, Calif.; William V. Fittipoldi, Philadephia; Orville M. Fitzgerald, Danville, Pa.; Louis Leo Flynn Jr., St. Paul; Estelle J. Foote, Waverley, Mass.; Burnell Gordon Forgey, Santa Monica, Calif.; Paul F. Franklin, Bronx, N. Y.; Charles Milford Gable, Seattle; Frank M. Gaines Jr., Louisville, Ky.; Stanford R. Gamm, Chicago; Raymond Harold Gehl, Newark, N. J.; Peter L. Giovacchini, Chicago; * Gilbert H. Glaser, New York; Abraham Glantzman Glenn, Brooklyn; Hilda C. Goldbach, Marcy, N. Y.; Albert Edward Goldberg, Forest Hills, N. Y.; Sidney S. Goldstein, West Kingston, R. I.; Maury Golob, Brooklyn; Bernard S. Gordon, Catonsville, Md.; * Warren F. Gorman, New York; Leon Gottfried, New York; William Gray, Boston; Wait Robbins Griswold, Vallejo, Calif.; Carl Michael Grossman, Los Angeles; Henry V. Guhleman Jr., Framingham, Mass.; Burte Guterman, Worcester, Mass.; James N. Haddock, Columbia, Mo.; Joel Stanley Handler, Chicago; Joseph Harvey Harris, Sacramento, Calif.; William Arthur Harvey, New York; Katharine Jaqueth Hawley, Waterbury, Conn.; Penrod Graham Hepfer, Coatesville, Pa.; Nathan L. Hoffenberg, Chicago; Frances Nan Howard, North Little Rock, Ark.; Albert Lester Ingram Jr., Wilmington, Del.; Charles W. Iobst, Bethlehem, Pa.; Avrohm Jacobson, Washington, D. C.; Samuel W. Joel, Boston; Edward D. Joseph, New York; Isadore Kamin, San Francisco; Isador J. Karlsberg, Quincy, Mass.; Myron Kass, Tacoma, Wash.; Jerome B. Katz, Topeka, Kan.; Bernhard Kaufman, Chicago; Jerome Kay, Delaware City, Del.; Abraham Kaye, Boston; Edgar A. P. Kellerman, New York; Edwin S. Kessler, Washington, D. C.; Franklin L. Kessler, White Plains, N. Y.; Jack L. Kinsey, New London, Conn.; Ernest S. Klein, Kankakee, Ill.; Peter Knowlton, Wynnewood, Pa.; Romuald J. Krajeski, San Francisco; Thaddeus P. Krush, Newton, Mass.; George L. Lake, West Brentwood, N. Y.; Vincent T. Lathbury, Philadelphia, Pa.; Paul Curtis Laybourne Jr., Kansas City, Kan.; David D. LeGrand, Baltimore; Robert James Lehman, West Brentwood, N. Y.; Julius Levine, Boston; Harvey Alvin Lewis, Chicago; Harold Isaiah Lief, Manhasset, N. Y.; Maurice E. Linden, Norristown, Pa.; Robert Lippert, Niles, Ill.; Werner O. Lippmann, Bangor, Maine; Barbara S. Lipton, Chicago; Ner Littner, Chicago; Albert Arthur Lorenz, Piedmont, Calif.; Harold Nager Lubing, Winnebago, Wis.; Henry H. Luster, Beverly Hills, Calif.; Lester MacLean, Chicago; Harold Earle Mann, Boston; James Mann, Boston; Henry F. Marasse, New York; * Sydney G. Margolin, New York; John J. Marren,

Tacoma, Wash.; Eugene M. Martin, New York; Harold R. Martin, Rochester, Minn.; Bernard Stephan Matthews, Cleveland; William Matthews McGaughey, Oakland, Calif.; William F. McLaughlin, Boston; Morton McMichael, Philadelphia; Stuart C. Miller, Stockbridge, Mass.; *Warren B. Mills, St. Louis; Russell R. Monroe, New Orleans; Robert Roy Morris, Rockville, Md.; Leon Moses, New York; Rocco L. Motto, Beverly Hills, Calif.; Warren J. Muhlfelder, New York; Joseph George Nemecek, Chicago; Edward C. Norman, Chicago; Gerald Bernard Olch, Norristown, Pa.; Leon Olinger, Brooklyn; Girardin S. O'Sullivan, Topeka, Kan.; Lilly Ottenheimer, New York; Roger D. Owen, Richmond, Calif.; Robert E. Peck, New York; Doris Phillips, Chicago; C. A. Pinderhughes, Framingham, Mass.; John McFarlane Rhoads, Philadelphia; William S. Robbins, Philadelphia; Jerman W. Rose, Utica, N. Y.; Allan J. Rosenberg, Palo Alto, Calif.; John R. Ross Jr., Syracuse, N. Y.; Mathew Ross, Beverly Hills, Calif.; Anthony P. Rousos, Perry Point, Md.; Arthur T. Rowe, Bronxville, N. Y.; Jack L. Rubins, New York; Marshall deGraffenried Ruffin, Washington, D. C.; Henry Harrison Sadler Jr., Detroit; Charles F. Samelson, Chicago; Isaac J. Sarfatty, Madison, Wis.; Elias Savitsky, New York; Marshall D. Schechter, Beverly Hills, Calif.; Irvine Schiffer, Waltham, Mass.; John L. Schimel, New York; Henry I. Schneer, New York; Lester Segal, Waco, Texas; Morey M. Segal, Chicago; Jerome M. Seides, Spring Valley, N. Y.; Lester Eli Shapiro, Rockville Centre, N. Y.; James E. Shea, New York; Edward Thomas Sheehan, Downey, Ill.; William R. Sheehy, Chicago; E. Rodman Shippen Jr., Melrose, Mass.; Rubin L. Siegel, New York; George A. Silver, Durham, N. C.; Pierre Charles Simonart, Philadelphia; Ralph Slater, New York; Jackson A. Smith, Houston, Texas; Herman B. Snow, Utica, N. Y.; Meyer Sonis, Philadelphia; William Stark, Washington, D. C.; Phillip H. Starr, St. Louis; Martin Steiner, San Francisco; Daniel H. Stephenson, Camden, N. J.; Margaret Olds Strahl, New York; Robert Cameron Sutton, Norristown, Pa.; Elliott H. Sweetser, Roxbury, Mass.; Harry Francis Tashman, New York; Graham Campbell Taylor, Pittsburgh; William C. Thompson, New Orleans; William Anthony Tillmann, London, Ont., Canada; Ellis E. Toney Jr., Los Angeles; Richard White Trevaskis Jr., Cumberland, Md.; George A. Ulett, St. Louis; Warren T. Vaughan Jr., Boston; Alexander S. Vujan, Philadelphia; Charles Waltner, Youngstown, Ohio; James Keene Ward, Birmingham, Ala.; Robert Allison Welch, Philadelphia; Joseph S. Weltman, Lexington, Ky.; Herbert B. Wender, Brooklyn; Robert Wexelblatt, Northport, N. Y.; Allen B. Wheelis, Stockbridge, Mass.; Mary Julian White, Washington, D. C.; Robert B. White, Stockbridge, Mass.; Charles Whitehill, New York; William Emmet Wilkinson Jr., Baltimore; Robert Orchard Willmott, Menlo Park, Calif.; Earl G. Witenberg, New York; John J. Wooster, Elgin, Ill.; Henry H. Work, Louisville, Ky.; George J. Wright Jr., New York; Nicholas Young, New York; Eugene L. Youngue Jr., Pittsburgh; Anthony Leon Zanni, Jamison, Pa.; Victor J. Zielinski, Chicago; Harold Zolan, Northport, N. Y.

Neurology.—Sidney Berman, New Haven, Conn.; Richard G. Berry, Bethesda, Md.; *Louis D. Boshes, Chicago; Gustave G. Gordon, Brooklyn; Warren V. Huber, San Antonio, Texas; Charles Arthur Kane, Bronx, N. Y.; John W. Kemble, Washington, D. C.; E. Charles Kunkle, Durham, N. C.; Robert Lee Lam, St. Louis; Tiffany Lawyer Jr., New York; Theodore Lipin, New York; *Leo Madow, Philadelphia; Marian Monica Millitzer, Long Beach, Calif.; Morton Nathanson, New York; E. Douglas Rooke, Rochester, Minn.; *Charles William Umlauf, Gladwyne, Pa.; William W. Wilson, Phildelphia.

Psychiatry and Neurology.—Kalman Frankel, Philadelphia; Harry H. Pennes, New York; Herta Seidemann, New York.

*The asterisk denotes supplementary certification.

THE NATIONAL PARAPLEGIA FOUNDATION

The National Paraplegia Foundation announces the continuation of a limited number of fellowships for research in spinal cord disease and trauma and in the complications commonly associated with such disease or injury. These fellowships carry a minimum stipend of $3,000 per year and may be awarded to any candidate who has demonstrated a capacity for medical

research and has outlined a program of meritorious study. The fellowships will be awarded by the Medical Advisory Committee and are open for award for the academic year 1951-1952. Application forms may be obtained from Dr. L. W. Freeman, chairman of the Medical Advisory Committee, and applications should be submitted to him not later than June 1, 1951.

THE AMERICAN ACADEMY OF FORENSIC SCIENCES

The American Academy of Forensic Sciences will hold its third annual meeting March 1, 2 and 3, 1951 at the Drake Hotel, Chicago. Communications should be addressed to the office of the president, Dr. R. B. H. Gradwohl, 3514 Lucas Avenue, St. Louis 3.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

At the thirtieth annual meeting of the Association for Research in Nervous and Mental Disease, held in New York on Dec. 15 and 16, 1950, the following officers were elected for the year 1951: president, Dr. S. Bernard Wortis; first vice president, Dr. John C. Whitehorn; second vice president, Dr. J. Lawrence Pool; secretary-treasurer, Dr. Clarence C. Hare; assistant secretary, Dr. Rollo Masselink.

Book Reviews

Schizophrenic Art: Its Meaning in Psychotherapy. By Margaret Naumburg, with preface by Thomas A. C. Rennie, M.D. Price, $10. Pp. 247, with 63 figures and 8 colored plates. Grune & Stratton, Inc., 381 4th Ave., New York 16, 1950.

For the past nine years, Maragaret Naumburg has done research in the field of art and psychotherapy. She describes the research project and the use of spontaneous art expression as a means of diagnosis and therapy. The descriptions and illustrations of this book center around the clinical study of the art products of two young schizophrenic patients. Spontaneous art expression is considered a supportive aid in the development of interpersonal relations.

Freud: Dictionary of Psychoanalysis. Edited by Nandor Fodor and Frank Gaynor, with a preface by Theodor Reik. Price, $3.75. Pp. 208. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1950.

This little book is a really astonishing item for the collector of curious publications. It looks like a new edition of a work by Freud, not showing the names of the two editors on the outside. The editors claim that the book supplies Freud's original terms and their proper definition in his own words, arranged in dictionary form. For the student of psychoanalysis and of Freud's work the reading of the book is painful. In many places it seems as though the editors had tried to make quotations appear utterly ridiculous. Most important theoretical and practical concepts are missing; frequently utterly irrelevant, and sometimes banal, statements are given considerable space. In the introduction, Theodor Reik compares psychoanalysis with the stable of King Augeas, which was dirtied by 3,000 oxen. Even if this comparison be true, the editors of this book have not lived up to a herculean job.

Modern Abnormal Psychology: The Definitive and Dynamic Aspects of the Abnormal, the Neuroses and Psychoses. Edited by William H. Miesell. Price, $10. Philosophical Library, Inc., 15 East 40th St., New York 16, 1950.

Designed to meet the interest of the general public in abnormal psychology, as well as the requirements of the student for a reference and source book, this comprehensive work tries to treat many aspects of many fields. The historical background of psychiatry and psychotherapy is discussed, along with a description of various neuroses and the principal psychoses. Diagnostic technics and the different forms of psychotherapy are outlined. The contributions are uneven in quality, and the editorial task is inadequately administered. Some of the chapters, such as Norman Brill's on psychopaths, Gabe and Grotjahn's on the history and present situation of medical psychotherapy, Sapirstein's on psychoanalysis and Zilborg's on psychosomatic medicine, are good examples of informative medical reporting.